





GENERAL PRINCIPLES  
OF  
ORGANIC SYNTHESSES

BY

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AUTHORIZED TRANSLATION WITH REVISION AND  
ADDITIONS

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TO THE GENERAL

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BY

**J. MERRITT MATTHEWS**

## PREFACE.

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THE present volume has been based on a monograph by Professor P. Alexeyeff (of the University of Kieff), entitled *Methods for the Transformation of Organic Compounds* (Методы Превращенія Органическихъ Соединеній), which originally appeared in 1889 in Russian. In the presentation of the subject in this volume, I have made rather extensive additions of new material, together with a general rearrangement of the entire subject-matter.

Professor Alexeyeff, himself, has been deceased these several years, but his widow, Madame Alexeyeff, has very kindly given me authority to employ her husband's book in the preparation of the present volume. I have also to thank Madame Alexeyeff for her kindness in placing at my disposal the originals of her husband's book in Russian, which have been of very material assistance to me in the translation. For the latter purpose I have also made good use of Darzen's and Lefèvre's French translation of the original Russian.

This book is intended for the general student of advanced organic chemistry, and deals only with the theory of the subject. It is not intended in any way as a laboratory manual for the preparation of organic compounds. Although there are a number of good books of the latter class available for the American or English student, yet I do not believe there is any book in English which covers quite the same ground as the present volume.

The attempt of the author has been to present the theory of organic radicals in a systematic form and in as logical a method of development as possible, so that the student may acquire a comprehensive grasp of the general principles underlying synthetic organic chemistry. General organic chemistry has grown so greatly in its mass of detail and in the number of its isolated reactions and separate compounds that the majority of advanced text-books on the subject are now more like complex reference encyclopedias than actual books of instruction. The student becomes bewildered in an attempt to pick his way through the thousands and thousands of compounds dealt with, and loses sight of the underlying path which represents the general principles of the subject. In the present book the author has endeavored to discuss general reactions in as broad a manner as possible, though making use of specific reactions for purposes of illustration. In such a treatment it is possible, of course, to become too purely theoretical and to make a few facts the basis of too generalized a reaction, and I fear that in many cases I have erred in this direction. This book, however, is intended to serve merely as a companion volume and to be used in connection with a general organic chemistry, and the latter will prevent the student from carrying too far the generalizations given in this volume.

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PHILADELPHIA, March, 1906.

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# GENERAL PRINCIPLES OF ORGANIC SYNTHESIS.

## CHAPTER I. OXIDATION.

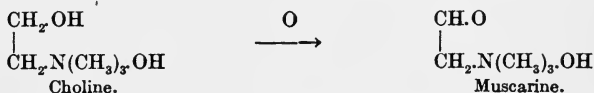
### I. GENERAL CONSIDERATIONS.

OXIDATION is one of the most important reactions in the synthesis of organic compounds. The element carbon has an especially strong attraction for oxygen, and nearly all organic compounds are more or less amenable to its action, either in a direct or an indirect manner. The compounds of the paraffin series, or, more properly, the open-chain series, are more susceptible to oxidation than those of the benzene or closed-ring series; and the extent to which the oxidation may be carried may vary within considerable limits, the final limit in all cases being the decomposition of the molecule into carbon dioxide and water.

Oxidation may operate in a large number of different directions, and by the use of an extensive series of reagents. In a number of instances the exact phase which the oxidation assumes will be dependent upon the nature of the reagent employed,<sup>1</sup> and many other conditions of the reaction; in some

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<sup>1</sup> When choline is treated with concentrated nitric acid, it is oxidized to muscarine:



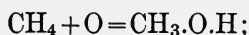
But when treated with either potassium permanganate or chromic acid mixture, negative results are obtained.

cases, it is possible to direct the mode and extent of the oxidation by a careful selection and proper regulation of the various conditions, and in this manner arrive at will at different results from the same starting-point. In other cases, the reaction is not so readily subject to control, and its variations may be very limited.

The elements and radicals occurring in organic compounds which are capable of oxidation, in one manner or another, are quite numerous. Carbon, as already mentioned, is especially susceptible to the action of oxygen; so also is hydrogen, and to a less degree sulphur and nitrogen, together with phosphorus and the allied elements which occur in a few of the carbon compounds. The halogens cannot be considered as oxidizable in the proper sense of the word. The various metals which may occur in organic combinations, in most instances, may be considered as subject to oxidation. But the majority of the reactions which have been carefully studied are limited to compounds including carbon, hydrogen, nitrogen, and sulphur as the elements subject to oxidation.

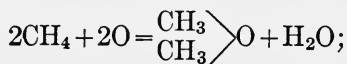
In the oxidation of the hydrocarbon nucleus (which in reality comes down to the methyl radical,  $\text{CH}_3$ , as the unit), both the hydrogen and the carbon may take part in the reaction. Starting with methane,  $\text{CH}_4$ , as the most highly-reduced compound of carbon, the following successive stages of oxidation may be indicated:

(1) The oxidation of a single hydrogen atom to an hydroxyl group:

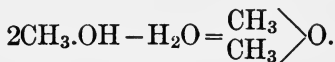


in this case but a single valence of the carbon atom is oxidized, and there is no removal of hydrogen.

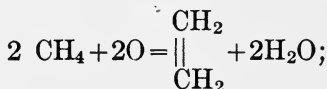
(2) The removal of a single hydrogen atom by oxidation to water, and the formation of the oxide of the radical:



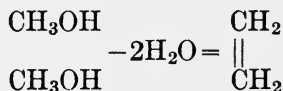
this reaction may be considered as the amplification of the foregoing:



(3) The removal of two hydrogen atoms in the form of water, and the formation of an unsaturated compound:



this reaction may also be considered as an amplification of the first:

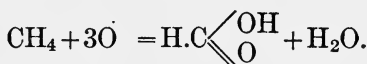


(4) The removal of two hydrogen atoms in the form of water and the simultaneous introduction of an oxygen atom in their place:



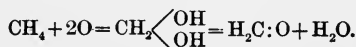
in this case, both the hydrogen and carbon are oxidized; the former to water and the latter to the carbonyl group, C:O, for the above compound is the aldehyde,<sup>1</sup>  $\text{H.C} \begin{array}{c} \diagup \text{H} \\ \diagdown \text{O} \end{array}$ .

(5) The oxidation and removal of two hydrogen atoms as water, and the simultaneous oxidation of another hydrogen atom to the hydroxyl group and of the carbon to the carbonyl group:

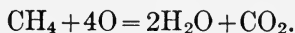



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<sup>1</sup> The intermediate reaction, that of the oxidation of two hydrogen atoms to hydroxyl groups without the elimination of water, does not appear to take place, as two hydroxyl groups cannot be attached to the same carbon atom, a molecule of water splitting off with the consequent formation of a carbonyl group:



(6) The oxidation and removal of all the hydrogen as water, and the simultaneous oxidation of the carbon to carbon dioxide:



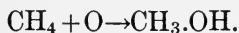
From the above considerations it may be seen that the oxidation of hydrocarbons may occur along the following general lines:

- (1) Oxidation by removal of hydrogen in the form of water.
- (2) Oxidation of hydrogen to hydroxyl.
- (3) Oxidation of carbon to carbonyl.<sup>1</sup>

In the first case, oxygen itself does not enter the molecule. This character of reaction is not a very general one, and when it does occur is usually brought about in an indirect manner. It leads to the formation of unsaturated compounds or condensation products.

In the last two cases, oxygen enters the molecule, but there is a difference in its mode of combination; in the second reaction only one valence of the carbon atom is held by oxygen, the second valence of the latter atom being attached to hydrogen (the hydroxyl group, alcohols) or to another similar element or group (the alcoholates,  $-\text{ONa}$ , the ethers,  $-\text{O.CH}_3$ , etc.). In the third reaction, both the valences of the oxygen atom are directly attached to the carbon to form the carbonyl group,  $=\text{C}:\text{O}$  (the aldehydes,  $-\text{HC}:\text{O}$ , the ketones,  $=\text{C}:\text{O}$ , and the acids,  $-\text{C}:\text{O.OH}$ ).

Some processes of oxidation occur with much more readiness than others; for instance, the direct oxidation of a hydrogen atom in a hydrocarbon nucleus to the hydroxyl group is rather rare, and will only take place under certain conditions:

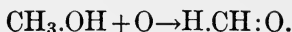


A group, however, already containing oxygen is more susceptible of oxidation as a rule. For instance, the alcohol,  $\text{CH}_3\text{OH}$ , is

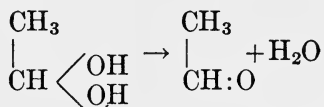
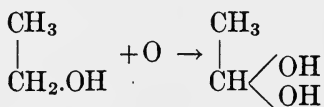
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<sup>1</sup> See also A. Wagner, *Action of Oxidants*, Warsaw, 1888 (Russian).

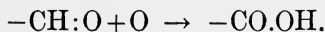
rather easily oxidized to the aldehyde:



§ In the case of compounds containing several hydrocarbon residues, it is recognized as a general law that when an alcohol is further oxidized the second oxygen atom becomes attached to the carbon atom already joined to the hydroxyl group. This causes the attachment of two hydroxyl groups to a single carbon atom, which is a very unstable grouping and immediately breaks down with the elimination of water and the formation of the carbonyl group:



In the case of primary alcohols containing the group  $-\text{CH}_2.\text{OH}$ , further oxidation causes the formation of aldehydes, having the group  $-\text{CH}:\text{O}$ ; with secondary alcohols, or those containing the group  $>\text{CH}.\text{OH}$ , ketones are formed with the group  $>\text{C}:\text{O}$ . In the case of tertiary alcohols, or those containing the group  $\begin{array}{c} \diagup \\ \text{C}.\text{OH} \\ \diagdown \end{array}$ , as there are no more hydrogen atoms capable of oxidation to hydroxyl, the molecule is broken down with the formation of acids having a less number of carbon atoms. As the aldehyde group still contains a hydrogen atom, it may be further oxidized with the formation of acids:



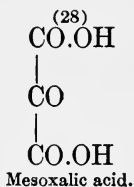
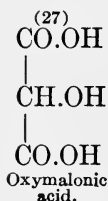
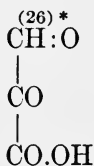
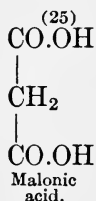
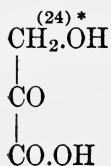
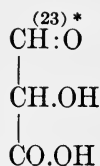
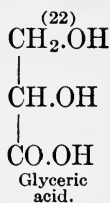
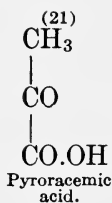
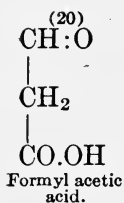
Ketones, on the other hand, cannot be further oxidized; if the oxidant employed is sufficiently powerful, the ketone is broken up into compounds having a less number of carbon atoms.

In order to show the various possibilities in the oxidation

of the methyl group, or its derivatives, the following list of the theoretical product of propane is given:<sup>1</sup>

$\begin{array}{c} \text{CH}_3 \\   \\ \text{CH}_2 \\   \\ \text{CH}_3. \end{array}$ Propane.	$\begin{array}{c} \text{(1)} \\ \text{CH}_2.\text{OH} \\   \\ \text{CH}_2 \\   \\ \text{CH}_3. \end{array}$ Primary propyl alcohol.	$\begin{array}{c} \text{(2)} \\ \text{CH}_3. \\   \\ \text{CH.OH} \\   \\ \text{CH}_3 \end{array}$ Secondary propyl alcohol.	$\begin{array}{c} \text{(3)} \\ \text{CH}_2.\text{OH} \\   \\ \text{CH.OH} \\   \\ \text{CH}_3 \end{array}$ Propylidene glycol.
$\begin{array}{c} \text{(4)} \\ \text{CH}_2.\text{OH} \\   \\ \text{CH}_2 \\   \\ \text{CH}_2.\text{OH} \end{array}$ Propylene glycol.	$\begin{array}{c} \text{(5)} \\ \text{CH:O} \\   \\ \text{CH}_2 \\   \\ \text{CH}_3 \end{array}$ Propyl-aldehyde	$\begin{array}{c} \text{(6)} \\ \text{CH}_3 \\   \\ \text{CO} \\   \\ \text{CH}_3 \end{array}$ Acetone.	$\begin{array}{c} \text{(7)} \\ \text{CH}_2.\text{OH} \\   \\ \text{CH.OH} \\   \\ \text{CH}_2.\text{OH} \end{array}$ Glycerol.
$\begin{array}{c} \text{(8)*} \\ \text{CH:O} \\   \\ \text{CH}_2 \\   \\ \text{CH}_2.\text{OH} \end{array}$	$\begin{array}{c} \text{(9)*} \\ \text{CH:O} \\   \\ \text{CH.OH} \\   \\ \text{CH}_3 \end{array}$	$\begin{array}{c} \text{(10)} \\ \text{CH}_2.\text{OH} \\   \\ \text{CO} \\   \\ \text{CH}_3 \end{array}$ Acetol.	$\begin{array}{c} \text{(11)} \\ \text{COOH.} \\   \\ \text{CH}_2 \\   \\ \text{CH}_3 \end{array}$ Propionic acid.
$\begin{array}{c} \text{(12)} \\ \text{CH}_2.\text{OH} \\   \\ \text{CH.OH} \\   \\ \text{CH:O} \end{array}$ Glyceric aldehyde.	$\begin{array}{c} \text{(13)*} \\ \text{CH}_2.\text{OH} \\   \\ \text{CO} \\   \\ \text{CH}_2.\text{OH} \end{array}$	$\begin{array}{c} \text{(14)*} \\ \text{CH:O} \\   \\ \text{CH}_2 \\   \\ \text{CH:O} \end{array}$	$\begin{array}{c} \text{(15)*} \\ \text{CH}_3 \\   \\ \text{CO} \\   \\ \text{CH:O} \end{array}$
$\begin{array}{c} \text{(16)} \\ \text{CH}_2.\text{OH} \\   \\ \text{CH}_2 \\   \\ \text{CO.OH} \end{array}$ Ethylene lactic acid.	$\begin{array}{c} \text{(17)} \\ \text{CH}_3 \\   \\ \text{CH.OH} \\   \\ \text{CO.OH} \end{array}$ Ethylidene lactic acid.	$\begin{array}{c} \text{(18)*} \\ \text{CH:O} \\   \\ \text{CH.OH} \\   \\ \text{CH:O} \end{array}$	$\begin{array}{c} \text{(19)*} \\ \text{CH:O} \\   \\ \text{CO} \\   \\ \text{CH}_2.\text{OH} \end{array}$

<sup>1</sup> Hjelt (trans. Tingle), *Principles of General Organic Chemistry*, p. 105.



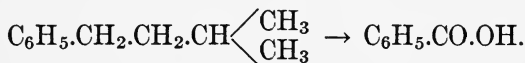
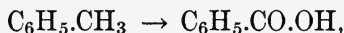
The compounds whose formulas are unnamed and marked with an asterisk have not yet been prepared.

Aromatic compounds, or those containing closed rings of carbon atoms, are not as readily oxidized in general as open-chain compounds. Oxidation of a compound containing a benzene ring, together with a side chain, usually results in the conversion of the latter into the carbonyl group; and it makes no difference how extensive or complicated the side-chain may be,<sup>1</sup>

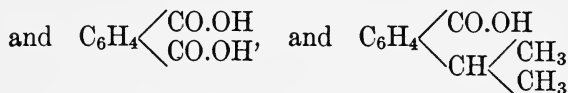
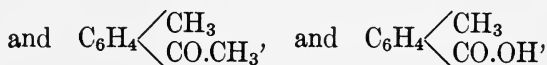
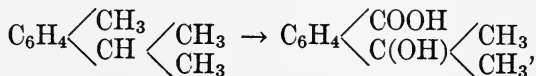
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<sup>1</sup> When several side-chains are present in aromatic compounds, their relative position in the molecule exerts considerable influence on the direction and extent of oxidation. For instance, dilute nitric acid does not oxidize metaxylene,  $\text{C}_6\text{H}_4(\text{CH}_3)_2$ , whereas it oxidizes paraxylene to paratoluic acid,  $\text{C}_6\text{H}_4\begin{array}{l} \text{CH}_3 \\ \diagup \\ \text{CO.OH} \end{array}$ . It is also to be observed that when a halogen atom is present in the benzene ring in the ortho-position to a methyl group, the latter does not as readily suffer oxidation with acid oxidants. (*Berichte*, vol. 24, p. 3778).

it will nearly always break down to the simple carbonyl group:



The reaction may sometimes be controlled by the use of mild oxidizing agents, as, for instance, in the oxidation of *cymene*:

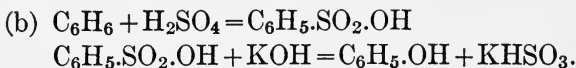
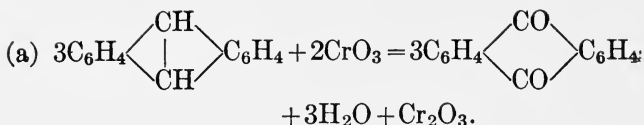


## II. ACTION OF OXIDIZING AGENTS.

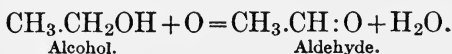
Oxidation may be brought about either *directly* by the action of a suitable oxidizing agent (as in the oxidation of anthracene to anthraquinone by the action of chromic acid) or *indirectly* through the formation of intermediate compounds (as in the preparation of phenol from benzene by first sulphonating the latter by treatment with sulphuric acid, and then fusing the sulphonic acid so obtained with caustic potash):<sup>1</sup>

<sup>1</sup> Lassar-Cohn makes the following remarks in regard to the carrying out of oxidations in organic chemistry: (a) When the product of oxidation is readily decomposed by the further action of the oxidant, it is frequently possible to add to the solution a carefully chosen extracting solvent, so that on the addition of the oxidant the whole may be shaken and the product removed from the influence of the latter by the solvent. The use of ice for the purpose of maintaining a low temperature also has a beneficial effect at times. (b) If the product of oxidation is volatile in steam, a current of the latter may be conducted through the solution during the oxidation. (c) In many cases where the preparation of a particular oxidized product is especially difficult, it is frequently possible to judiciously choose some derivative of the substance to be operated on, which by proper treatment will yield the same product.—*Manual of Organic Chemistry* (trans. Smith), p. 244.





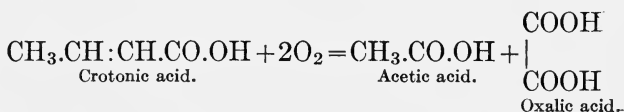
Oxidation may also occur in two different directions: (a). The compound may contain the same number of carbon atoms after oxidation as before:



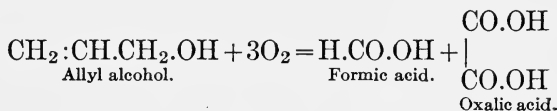
(b) The oxidation may be accompanied by a decomposition of the molecule, with the formation of two or more substances containing fewer carbon atoms than the original compound:



This latter form of oxidation is especially liable to occur with the unsaturated compounds of the aliphatic series, as in the oxidation of crotonic acid to a mixture of acetic and oxalic acids,



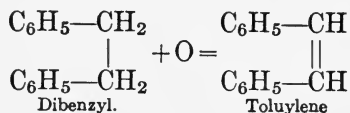
or of allyl alcohol to formic and oxalic acids:



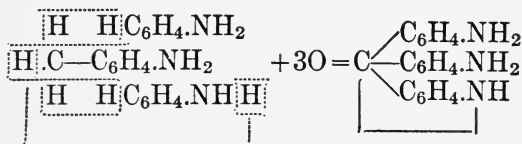
In such cases the compound, as a rule, breaks down at the position of the double bond.

In some reactions, oxidation may result in the condensation of the compound, either in its own molecule or with other substances, by reason of the elimination of hydrogen by the oxygen.

For instance, the oxidation of dibenzyl leads to the formation of toluylene:



The formation of pararosaniline by the oxidation of a mixture of aniline and paratoluidine is also an illustration of this reaction:



A large number of different bodies may be employed as oxidants, though the action of different oxidants may vary considerably towards the same organic compound. The oxidation of aniline by various oxidants may be taken as an illustration. When treated with a mixture of manganese dioxide and sulphuric acid, aniline yields ammonia and a small amount of quinone.<sup>1</sup> When oxidized with chromic acid mixture, however, a quantitative yield of quinone is obtained; with an alkaline solution of potassium permanganate, aniline is converted into azo-benzene, ammonia, and oxalic acid;<sup>2</sup> whereas, in an acid solution, the same oxidant gives aniline black, and, in a neutral solution, nitro-benzene and azo-benzene are formed;<sup>3</sup> boiled with a solution of bleaching-powder,<sup>4</sup> aniline gives nitro-benzene; with an acid solution of hydrogen peroxide, ammonia

<sup>1</sup>  $\text{C}_6\text{H}_5\text{.NH}_2 + \text{O}_2 = \text{C}_6\text{H}_4\text{O} + \text{NH}_3$ .

<sup>2</sup>  $3\text{C}_6\text{H}_5\text{.NH}_2 + 5\text{O} = \text{C}_6\text{H}_5\text{N:N.C}_6\text{H}_5 + \text{NH}_3 + (\text{COOH})_2 + \text{H}_2\text{O}$ .

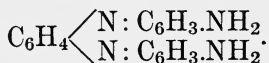
<sup>3</sup>  $3\text{C}_6\text{H}_5\text{.NH}_2 + 3\text{O} = \text{C}_6\text{H}_5\text{.N:N.C}_6\text{H}_5 + \text{C}_6\text{H}_5\text{.NO}_2 + 3\text{H}_2\text{O}$ .

<sup>4</sup> Ortho-nitrobenzal-acetone is converted into ortho-nitro-cinnamic acid by the oxidizing action of sodium hypochlorite (mixture of bleaching-powder and

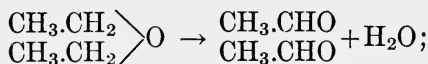
and dianilido-benzoquinone-anilide is formed; while, in a strong acid solution, the same oxidant gives an induline derivative.<sup>1</sup>

The following summary gives the principal oxidizing agents employed, together with a brief account of their action:<sup>2</sup>

**Oxygen** acts directly only on easily oxidizable substances. Air, when acting in the presence of heated platinum or platinum sponge, will oxidize primary alcohols to aldehydes, and even aldehydes themselves are gradually converted into acids. Formaldehyde, for instance, may be prepared by conducting a mixture of methyl alcohol vapor and air over a heated platinum spiral. The hydrochloride of paraphenylene-diamine is easily oxidized by exposure to the air, giving almost a theoretical yield of tetra-amido-diphenyl-para-azophenylene:



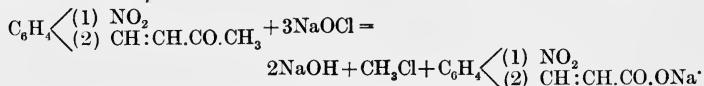
By passing the vapors of many substances mixed with air over a heated spiral of copper superficially oxidized, oxidation products are obtained, as a rule, more readily than with a platinum spiral. Ethyl ether, for instance, is oxidized to aldehyde,



and toluene gives benzaldehyde:



sodium carbonate):



<sup>1</sup> Benzylidene-acetone is converted into cinnamic acid by the oxidizing action of bromine in alkaline solution. The oxidizing action of bromine has also been made use of among the carbohydrates; for instance, by heating milk-sugar with bromine an acid is formed; by heating glycerol with bromine and soda-ash, glycerose is formed.

<sup>2</sup> For a detailed discussion of the different oxidizing agents employed in organic syntheses, see Lassar-Cohn, *Manual of Organic Chemistry*, pp. 243-286.

**Silver oxide** in alkaline solution readily oxidizes aldehydes to acids, with the precipitation of metallic silver:



Glycerol is converted into glycollic acid. The ammoniacal solution of silver oxide for the testing of aldehydes is best prepared by mixing a solution of 10 parts silver nitrate in 100 parts water with one of 10 parts caustic soda in 100 parts water, and then adding ammonia-water drop by drop until the precipitate of silver oxide has completely dissolved. The solution should be kept in a dark place.

**Manganese dioxide** is used in connection with sulphuric acid for oxidation in acid solutions. When the vapor of alcohol is conducted over pyrolusite heated to 150–360° C., it is mostly converted into acetone.

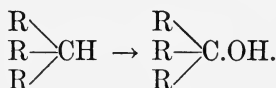
**Potassium permanganate** is perhaps more frequently used than any other oxidizing agent. It may be employed in neutral, acid, or alkaline solution.<sup>1</sup> In neutral solution it acts as follows:



In alkaline solution the reaction is the same. In acid solution it is as follows:



Compounds containing hydrogen, linked to a tertiary carbon atom, have the hydrogen converted into hydroxyl by the action of an alkaline solution of potassium permanganate:



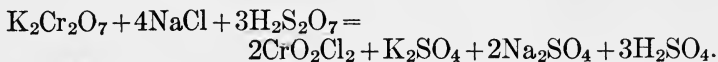
<sup>1</sup> Reichardt, in his investigations on the action of different oxidizing agents on soluble starch, found that potassium permanganate in acid, alkaline, and neutral solutions, and chromic acid, have an energetic action, but all give rise to indefinite, dirty-brown products; chlorine and alkaline copper hydrate solution gave the same result; but by warming the starch solution with bromine and afterwards treating the product with silver oxide, gluconic acid was obtained. Starch heated with nitric acid gave carbon dioxide and oxalic acid, whereas fuming nitric acid gave a mono-nitro-derivative.

The group  $=\text{CH}_2$  is usually converted into CO by the action of potassium permanganate.

**Chromic acid** is extensively used for the preparation of aldehydes, ketones, and acids from alcohols; for the oxidation of aromatic hydrocarbons (with the exception of the ortho-compounds), and for the preparation of quinones. Chromic acid is almost always used in acetic acid solution, as, when dissolved in water, it gives a precipitate of chromic oxide.<sup>1</sup> A mixture of potassium bichromate and sulphuric acid may also be used; this is known as "chromic acid mixture." For the oxidation of the aromatic hydrocarbons, a mixture of 4 parts  $\text{K}_2\text{Cr}_2\text{O}_7$  and 6 parts  $\text{H}_2\text{SO}_4$ , diluted with twice its volume of water, is found to be most suitable. In the case of alcohols a more dilute solution is necessary. Many compounds, such as oxyacids, ketones, etc., may be decomposed by chromic acid mixture, with the formation of products containing less carbon atoms. A mixture of potassium bichromate and acetic acid is sometimes used; other acids may also be substituted. The oxidizing power of these mixtures is calculated on the principle that the  $\text{CrO}_3$  is converted into  $\text{Cr}_2\text{O}_3$ :

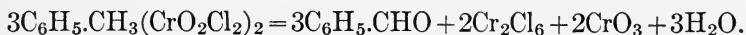


**Chromyl chloride** is another useful oxidizing agent, especially for converting the methyl groups in aromatic hydrocarbons into aldehyde groups. Thus, nitrotoluene is converted into nitrobenzaldehyde. Chromyl chloride is prepared by acting on a mixture of salt and potassium bichromate with fuming sulphuric acid:



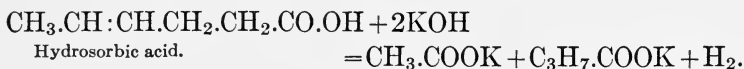
<sup>1</sup> The formation of the oxide may sometimes interfere with the proper course of the reaction, especially in the case of organic acids, where the latter may combine with the oxide. Should the solution of chromic acid in water be used, it is best to acidify it with sulphuric or hydrochloric acid. The use of an acetic acid solution, however, is further favored by the fact that many of the bodies which it is the purpose to oxidize may be dissolved therein, and the speed of oxidation then regulated by gradual addition of chromic acid.

The action of chromyl chloride is very violent, and it must be used in carbon disulphide solution. It is probable that at first double compounds are formed between the hydrocarbons and the chromyl chloride, which are decomposed by water with the formation of aldehydes:

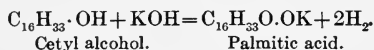


**Nitric acid** may be used as an oxidant, though it also has a nitrating action. When employed as an oxidant, nitric acid diluted with two molecules of water is generally used; such an acid acts less energetically than chromic acid mixture. Concentrated nitric acid usually converts compounds of the methane series into oxalic acid or carbon dioxide.

**Caustic potash** acts as an oxidant when it is fused with the substance. The higher primary alcohols in this manner yield acids. Phenols, when fused at high temperatures with caustic potash, give diphenols.<sup>1</sup> Unsaturated compounds are usually decomposed by fusion with caustic potash, the carbon chain being broken at the position of the double bond, the products being oxidized to acids. Hydrosorbic acid, for instance, gives acetic and butyric acids:



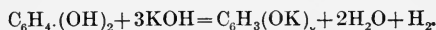
<sup>1</sup> Oxidation produced through fusion with caustic potash is a peculiar one. Primary alcohols are converted directly into acids:



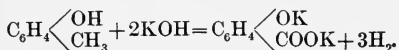
Phenols are also oxidized by the same means at high temperatures, the reaction varying with the composition of the phenol, hydrogen being evolved in each case. Phenol, for example, gives diphenol:



Resorcinol gives diresorcinol and some phloroglucinol:



With cresol, the side-chain is oxidized:



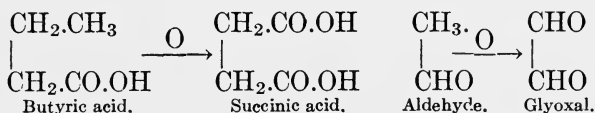
### III. DIRECT OXIDATION.

#### A. Oxidations which Preserve the Same Number of Carbon Atoms in the Molecule.

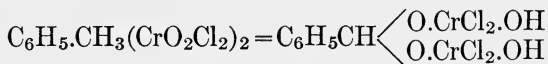
Attention has already been drawn to the fact that oxidation may be either direct or indirect, and that the former mode may in turn be subdivided into (1) oxidation which preserves the same number of carbon atoms in the molecule, and (2) oxidation accompanied by a greater or less destruction or breaking-down of the molecule. When the destruction of the body is complete, with the formation of carbonic acid, the oxidation is termed *combustion*.

The various radicals or groups to be met with in organic chemistry will now be examined with reference to their behavior with oxidants.

The  $-\text{CH}_3$  group is oxidized almost exclusively only in aromatic compounds. It is then changed into the aldehyde group,  $-\text{CHO}$ , or the carboxyl or acid group,  $-\text{CO.OH}$ . It is difficult to cite any examples in the paraffin series of the oxidation of the  $-\text{CH}_3$  group into  $-\text{CHO}$  or  $-\text{CO.OH}$ ; about the only cases known are the conversion of butyric acid into succinic acid, and the production of glyoxal by the oxidation of aldehyde:

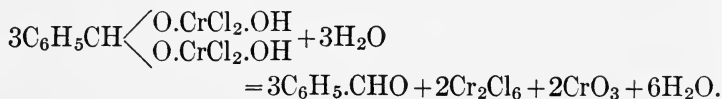


The  $\text{CH}_3$  group is converted into  $\text{CHO}$ <sup>1</sup> by decomposing with water the double compounds of the aromatic hydrocarbons with chromyl chloride. The compound with toluene, for example, should apparently be represented by the following formula:



<sup>1</sup> The oxidation of the  $\text{CH}_3$  group into  $\text{CHO}$  may be effected by employing air in the presence of an oxidized copper spiral (Löw, *Jour. pr. Chem.*, vol. 91 p, 323). By this means toluene,  $\text{C}_6\text{H}_5.\text{CH}_3$ , is converted into benzaldehyde,  $\text{C}_6\text{H}_5.\text{CHO}$ . (See above.)

The decomposition with water evidently proceeds in accordance with the following equation:



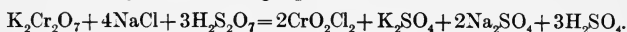
The operation is carried out in the following manner:<sup>1</sup>

Dissolve 1 part (1 mol.) of the hydrocarbon in 7 parts of carbon disulphide, and gradually add, with cooling, 10–15 parts of a solution of 1 part (2 mols.) of chromyl chloride in 7 parts of carbon disulphide; after each addition wait until the red coloration has disappeared. The precipitate is collected on some glass wool, washed with carbon disulphide, and dried on a water-bath. It is then decomposed by gradually pouring into cold water, and the aldehyde is removed by means of ether. The aldehyde may also be isolated by treating the solution with a current of sulphur dioxide gas. Chromyl chloride, acting on aromatic hydrocarbons with side-chains, transforms them into aldehydes; with benzene, however, quinone is formed.

By the aid of chromyl chloride, not only can the **CH<sub>3</sub>** group in hydrocarbons be transformed into **CHO**, but also in their derivatives. For instance, the compound propylphenyl-ketone,  $\text{C}_6\text{H}_5.\text{CO}.\text{CH}_2.\text{CH}_2.\text{CH}_3$ , when oxidized, gives benzoyl-propylic aldehyde,  $\text{C}_6\text{H}_5.\text{CO}.\text{CH}_2.\text{CH}_2.\text{CHO}$ .<sup>2</sup>

The **CH<sub>3</sub>** group in aromatic compounds is converted into **CO.OH** by the action of most oxidants. In this manner the hydrocarbons are transformed into organic acids either by dilute

<sup>1</sup> Chromyl chloride is prepared in the following manner: Fuming sulphuric acid is added to a mixture of common salt and potassium bichromate in the proportions indicated by the following equation:



The mixture is distilled from a large flask until the contents begin to foam. A secondary reaction, resulting in the liberation of chlorine, proceeds according to the following equation:

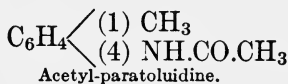


<sup>2</sup> Bureker, *Ann. de Chem. et de Phys.*, vol. 26, p. 470.

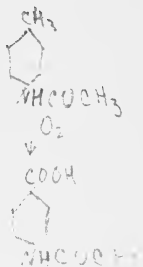
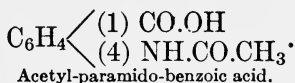


nitric acid, chromic acid mixture,<sup>1</sup> potassium permanganate, or even by fusion with caustic potash. The fusion with caustic potash is principally employed for the purpose of oxidizing the  $\text{CH}_3$  group in phenols. This fusion should be carried out at a temperature of  $200\text{--}250^\circ \text{C}$ . for several hours; 4 to 5 parts of caustic potash (KOH), moistened with a little water, are used for 1 part of phenol. The end of the reaction is indicated by the liberation of hydrogen ceasing.

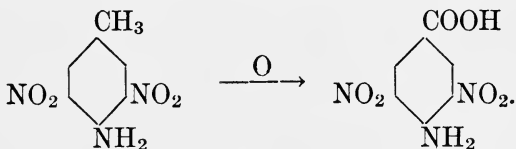
In the case of amido derivatives, the  $\text{NH}_2$  group should be preserved against the action of oxidants by the introduction of an acid radical; otherwise there would result quinones and azo-compounds. Thus,



gives, on oxidation,



The presence of the  $\text{NO}_2$  group often protects the  $\text{NH}_2$  group from oxidation: thus, dinitrotoluidine, on oxidation with chromic acid mixture, gives amido-dinitro-benzoic acid:



Frequently different oxidants do not behave in the same manner. Thus orthotoluic acid,  $\text{C}_6\text{H}_4 \begin{matrix} \text{CH}_3 \\ \text{COOH} \end{matrix} \begin{matrix} (1) \\ (2) \end{matrix}$ , gives phthalic acid when oxidized by potassium permanganate; but when treated with chromic acid mixture it is completely decomposed

<sup>1</sup> In place of chromic acid mixture (4 parts potassium bichromate and 5 parts sulphuric acid) there may be employed a solution of chromic acid in glacial acetic acid.

into carbonic acid. In the same way cymene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{(1) CH}_3 \\ \text{(4) C}_3\text{H}_7 \end{smallmatrix}$ , by the oxygen of the air (as in the animal organism), is transformed into cuminic acid,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{(1) COOH} \\ \text{(4) C}_3\text{H}_7 \end{smallmatrix}$ , by the oxidation of the  $\text{CH}_3$  group and transformation of the  $\text{C}_3\text{H}_7$  group into its isomeric form; but when oxidized with dilute nitric acid, it is the  $\text{C}_3\text{H}_7$  group which is attacked, and paratoluic acid is produced,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{(1) CH}_3 \\ \text{(4) COOH} \end{smallmatrix}$ , which on further oxidation yields terephthalic acid,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{(1) COOH} \\ \text{(4) COOH} \end{smallmatrix}$ . When the aromatic hydrocarbon contains groups other than  $\text{CH}_3$  and of the formula  $\text{C}_n\text{H}_{2n+1}$ , they are oxidized like  $\text{CH}_3$  and are all transformed into  $\text{COOH}$ . Thus, ethyl-benzene,  $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CH}_3$ , on oxidation gives benzoic acid,  $\text{C}_6\text{H}_5\cdot\text{COOH}$ . If, besides these groups, the hydrocarbon contains another side-chain of  $\text{CH}_3$ , the latter is oxidized subsequently, as in the case of the oxidation of cymene to paratoluic acid, and then to terephthalic acid.

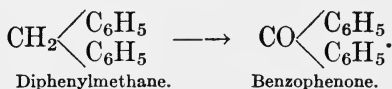
The presence of the **acid groups**,  $\text{NO}_2$ ,  $\text{COOH}$ ,  $\text{SO}_2\text{OH}$ , renders the oxidation more difficult. Thus, while toluene,  $\text{C}_6\text{H}_5\text{CH}_3$ , and its mono-chlor derivative,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{Cl} \\ \text{CH}_3 \end{smallmatrix}$ , are easily oxidized by the action of dilute nitric acid, nitro-toluene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{NO}_2 \\ \text{CH}_3 \end{smallmatrix}$ , is only oxidized by chromic acid mixture, or by heating with dilute nitric acid in a sealed tube; and the corresponding dinitro-derivative,  $\text{C}_6\text{H}_3 \begin{smallmatrix} \text{(NO}_2\text{)}_2 \\ \text{CH}_3 \end{smallmatrix}$ , is not oxidized by even chromic acid mixture.

If the  $\text{CH}_3$  is in the **ortho** (1:2) position with an acid group, it cannot be oxidized by either nitric acid or chromic acid mixture; it is necessary to use potassium permanganate in alkaline solution, or fusion with potash.

Furthermore, it should be noted that in the oxidation of unsymmetrical pseudocumene,  $\text{C}_6\text{H}_3(\text{CH}_3)_3(1:2:4)$ , by dilute nitric acid, there are formed two isomeric acids,  $\text{C}_6\text{H}_3 \begin{smallmatrix} \text{COOH} \\ \text{(CH}_3\text{)}_2 \end{smallmatrix}$ .

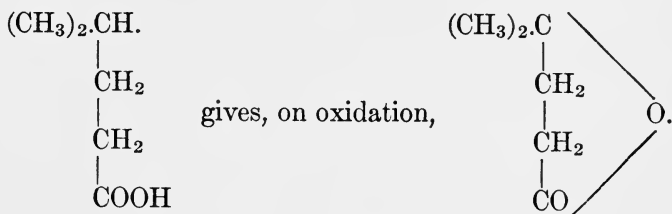
xylylic and paraxylylic acids, according to which  $\text{CH}_3$  is oxidized; but in the oxidation of the symmetrical hydrocarbon, mesitylene,  $\text{C}_6\text{H}_3(\text{CH}_3)_3(1:3:5)$ , there is only one acid obtained, mesitylenic acid,  $\text{C}_6\text{H}_3\left\langle \begin{smallmatrix} \text{COOH} \\ (\text{CH}_3)_2 \end{smallmatrix} \right\rangle$ , as may be readily understood. ✓

The  **$\text{CH}_2$  group** in aromatic compounds is oxidized and converted into the **carbonyl group,  $\text{CO}$** , by means of chromic acid mixture, solution of chromic acid in acetic acid, or dilute nitric acid. In this manner the ketones are obtained:



The  **$\text{CH}_2$  group** undergoes oxidation even in preference to the  $\text{CH}_3$  group. Thus, by the action of a solution of chromic acid in acetic acid, ethylbenzene gives, simultaneously with benzoic acid, the ketone  $\text{C}_6\text{H}_5.\text{CO}.\text{CH}_3$ .

The  **$\text{CH}$  group** is characterized by the ease with which it is converted into the tertiary alcohol group,  **$\text{C.OH}$** , which is true not only in aromatic compounds, but also in the paraffins. Thus, isobutyric acid,  $\text{CH}(\text{CH}_3)_2.\text{COOH}$ , by the action of an alkaline solution of potassium permanganate is converted into oxy-isobutyric acid,  $\text{C}(\text{OH})(\text{CH}_3)_2.\text{COOH}$ . Cuminic acid behaves in the same manner, being converted into oxycuminic acid. When the  **$\text{CH}$**  is in the  $\gamma$ -position to a carboxyl group, instead of obtaining an hydroxy-acid on oxidation, a ketone is formed by the splitting-off of water.



By the same method of oxidation as above, the compound

$\text{C}_6\text{H}_3 \begin{cases} \text{CH}_3 \\ \text{SO}_2\text{OH} \\ \text{CH}(\text{CH}_3)_2 \end{cases}$  gives  $\text{C}_6\text{H}_3 \begin{cases} \text{CH}_3 \\ \text{SO}_2\text{OH} \\ \text{C}(\text{OH})(\text{CH}_3)_2 \end{cases}$  ; but if dilute ni-

tric acid is used as the oxidant, there is formed  $\text{C}_6\text{H}_3 \begin{cases} \text{CH}_3 \\ \text{SO}_2\text{OH} \\ \text{COOH} \end{cases}$

instead. Triphenylmethane,  $\text{CH}(\text{C}_6\text{H}_5)_3$ , is converted into triphenylcarbinol,  $\text{C}(\text{OH})(\text{C}_6\text{H}_5)_3$ , by the action of chromic acid.

The **CH** group, which forms a part of the closed benzene ring, on the contrary is oxidized with difficulty, and in the majority of cases only by indirect means. Benzene is converted into phenol by oxygenated water, or by oxygen in the presence of aluminium chloride; in the presence of sulphuric acid, benzene gives quinone by the action of oxygenated water.

The presence of **OH** in benzene renders the **CH** more susceptible to oxidation; phenol,  $\text{C}_6\text{H}_5\text{OH}$ , on fusion with soda in the air, gives pyrocatechol, and resorcin yields phloroglucol; polyhydric phenols in alkaline solution combine energetically with the atmospheric oxygen, giving, among other products, acetic acid and carbon dioxide.

The conversion of the group  $\begin{array}{c} \text{CH} \\ | \\ \text{CH} \end{array}$  into  $\begin{array}{c} \text{CO} \\ | \\ \text{CO} \end{array}$  in the compounds

of the type  $\text{R}'' \begin{array}{c} \text{CH} \\ | \\ \text{CH} \end{array} \text{R}''$  and  $\begin{array}{c} \text{CH} \\ || \\ \text{CH} \end{array} \text{R}''$ , as anthracene,

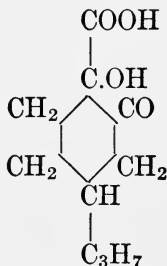
$\text{C}_6\text{H}_4 \begin{array}{c} \text{CH} \\ | \\ \text{CH} \end{array} \text{C}_6\text{H}_4$  and phenanthrene  $\begin{array}{c} \text{CH}-\text{C}_6\text{H}_4 \\ || \\ \text{CH}-\text{C}_6\text{H}_4 \end{array}$  can be explained

by admitting the formation of  $2(\text{C}(\text{OH}))$ , which fixes  $\text{O} + \text{H}_2\text{O}$ , and then splits off water,  $2\text{H}_2\text{O}$ . Thus, with anthracene there

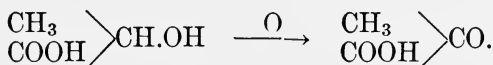
is first formed,  $\text{C}_6\text{H}_4 \begin{array}{c} \text{C} \text{---} \text{O} \text{H} \\ | \quad | \\ \text{C} \text{---} \text{O} \text{H} \\ | \quad | \\ \text{C} \text{---} \text{O} \text{H} \\ | \quad | \\ \text{C} \text{---} \text{O} \text{H} \end{array} \text{C}_6\text{H}_4$ , then  $2\text{H}_2\text{O}$  is eliminated.

It is doubtless by the aid of an analogous reaction that terebenthene,  $\text{C}_{10}\text{H}_{16}$ , is transformed into camphor,  $\text{C}_{10}\text{H}_{16}\text{O}$ ,

and the latter is itself transformed into camphoric acid, which would not be formed by the simple fixation of oxygen. For it has been shown by Friedel<sup>1</sup> that camphoric acid is not a dibasic acid, but a compound of alcohol, ketone, and acid, as is indicated by the formula:



The **CH.OH** group is easily oxidized to **CO**, by nitric acid, chromic acid, potassium permanganate, or chromic acid mixture. In these reactions there are frequently obtained secondary products arising from the decomposition of the compounds at first formed. In this manner, secondary alcohols are converted into ketones by the action of oxidants; lactic acid, by reason of its **CH.OH** group, gives pyruvic acid with potassium permanganate:

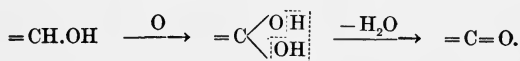


The **CHOH** group in certain cases is oxidized even more readily than the **CH<sub>2</sub>.OH** of primary alcohols; the oxidation

of phenyl-glycol,  $\begin{array}{c} \text{C}_6\text{H}_5.\text{CH.OH} \\ | \\ \text{CH}_2.\text{OH} \end{array}$ , gives the ketone-glycol  $\begin{array}{c} \text{C}_6\text{H}_5.\text{CO} \\ | \\ \text{CH}_2\text{OH} \end{array}$ , together with a small quantity of ketonic acid,

<sup>1</sup> *Bull. Soc. Chim.*, 1889, p. 83.

<sup>2</sup> This reaction may be considered as taking place in the following manner:



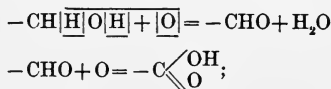
$\text{C}_6\text{H}_5\text{CO}$  . In the case of saturated polyhydric alcohols,  
 $\begin{array}{c} | \\ \text{COOH} \end{array}$

the contrary is true, and the  $\text{CH}_2\text{OH}$  is oxidized; in this manner aldehydic acids may be prepared. Thus, erythrite yields erythric acid:

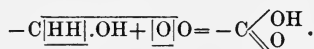


The  $\text{CH}_2\text{OH}$  group on oxidation is changed into  $\text{CO.OH}$  or  $\text{CHO}$ .<sup>1</sup> It is converted into  $\text{CO.OH}$  by the action of numerous oxidants, and, in certain cases, by the action of atmospheric oxygen in the presence of platinum black.<sup>2</sup> It was in this manner that Grimaux<sup>3</sup> prepared the first synthetic sugar by oxidizing glycerol. Primary alcohols by this means can be converted into acids. The action of the platinum black is at times too energetic, and the reaction must be moderated by diluting the alcohol with water. If the alcohol is very volatile,

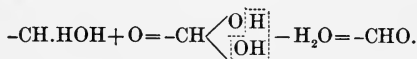
<sup>1</sup> The mechanism of these reactions is as follows:



the alcohol group may also be considered in some cases as being directly oxidized to the acid, as follows:



This is a very probable assumption, because the H in the hydroxyl group of the alcohol is already oxidized, and when the acid is formed directly it is more likely that the two H's of the nucleus are oxidized and removed, rather than one H from the nucleus and one from the hydroxyl group. In fact, the first oxidation of the alcohol group to the aldehyde may be more logically considered as:



<sup>2</sup> The  $\text{CH}_2\text{OH}$  group may be oxidized to the  $\text{CHO}$  group by means of air in the presence of platinum. (Hofmann, *Ann.*, vol. 145, p. 358; Tollens, *Ber.*, vol. 19, p. 2133.) This was the first method employed for the preparation of formaldehyde,  $\text{H}.\text{CHO}$ , from methyl alcohol,  $\text{CH}_3.\text{OH}$ . Superficially oxidized copper has been found to be even more effective than platinum. (Löw, *Jour. pr. Chem.*, vol. 141, p. 323.)

<sup>3</sup> *Bull. Soc. Chim.*, vol. 45, p. 481.

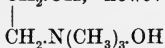
place it in a beaker beside another one containing the platinum black, and cover the whole with a watch-glass.

The  $\text{CH}_2\text{OH}$  group is converted into  $\text{CHO}$  usually by means of chromic acid mixture, this being the customary method of preparing aldehydes. It is necessary to take a slightly less quantity of alcohol than the theoretical amount.<sup>1</sup> As secondary products, there are obtained acetals and ethers by reason of a more advanced oxidation giving rise to some acid which reacts on the alcohol. The aromatic aldehydes are often obtained in a different manner. The chloride corresponding to the alcohol does not yield the latter very readily, but it may be directly transformed into the aldehyde by heating with a nitrate, and lead nitrate in particular. It may be that the nitric ether, which is at first formed, is saponified by the water, and the nitric acid thus liberated oxidizes the alcohol into the aldehyde. In order to obtain aldehydes by the decomposition of ordinary ethers, see p. 55; and for the action of quinone on alcohol, see p. 54.

The  $\text{CHO}$  group of aldehydes is oxidized to  $\text{CO.OH}$  by the action of chromic acid mixture, alkaline solution of potassium permanganate, etc., or by gradually adding to the solution of the aldehyde in glacial acetic acid the theoretical amount of chromic acid dissolved in the same solvent. The unsaturated aldehydes are easily oxidized by the action of silver oxide.

Aldehydes are also oxidized directly by atmospheric oxygen:

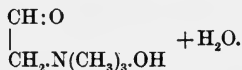
<sup>1</sup> The  $\text{CH}_2\text{OH}$  group in choline,  $\text{CH}_2\text{OH}$ , however, gives negative re-



sults when efforts are made to oxidize it with potassium permanganate or with chromic acid. With concentrated nitric acid, however, muscarine,

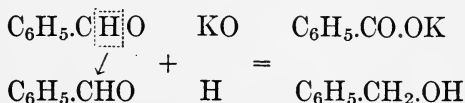
$\begin{array}{c} \text{CH} \begin{array}{l} \text{OH} \\ \text{OH} \end{array} \\ | \\ \text{CH}_2\text{N}(\text{CH}_3)_3\text{OH} \end{array}$ , was easily obtained. Like other similar bodies, this formula

for muscarine is open to doubt: it probably has the form of the customary aldehyde:

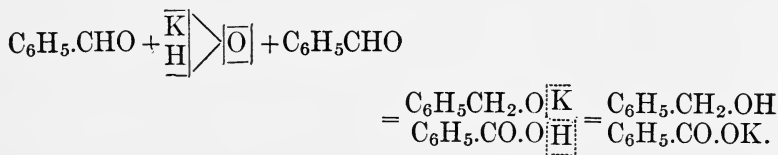


thus vanillin, on exposure to the air, is gradually converted into vanillic acid; benzoic aldehyde, into benzoic acid;  $\alpha$ -naphthoic aldehyde, very easily into  $\alpha$ -naphthoic acid, etc.

The aromatic aldehydes are oxidized in the air by fusion with caustic potash, and often even by the action of an alcoholic solution of potash. In the latter reaction there is formed at the same time the reduction product of the aldehyde:



This reaction is peculiarly interesting in that it presents an oxidation and a reduction proceeding simultaneously on the same substance. It seems rather difficult to understand just how a hydrogen atom migrates so illogically from one molecule to another. It may be that the reaction takes place after this fashion:



In order to effect this reaction it is necessary to employ a very concentrated solution of caustic potash, and allow the mixture to stand for several hours, taking care not to allow the temperature to rise too high. After diluting with water, the alcohol is removed with ether, and the acid is obtained from its aqueous solution.

In the paraffin series this reaction gives resins and condensation products. Like the aromatic aldehydes, glyoxal is reduced by alcoholic potash, giving glycollic acid.

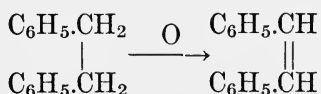
All the cases of oxidation which have been met with so far may be considered as a fixation of oxygen, or as a replacement by OH of a hydrogen united to carbon. It has not yet been possible to fix oxygen to the carbon in unsaturated compounds,



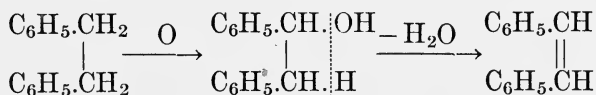
with the exception of carbon monoxide. By passing a current of strongly ozonized dry air through anhydrous ether, ethyl peroxide is formed,  $\text{C}_2\text{H}_5.\text{O.O.C}_2\text{H}_5$ , a liquid which decomposes on heating, and reacts with water to form alcohol and hydrogen peroxide.

The conversion of cyanides into cyanates presents an example of changing from the metallic radical into .OM, analogous to the transformation of H into .OH.

If the transformation of alcohols into aldehydes, etc., however, is not a simple removal of hydrogen, there are cases where oxygen causes the removal of hydrogen. The body then combines with itself; in this manner there are formed bisulphides, pinacones, etc., or a double linking is formed between two carbon atoms. Thus, by passing the vapor of dibenzyl over heated lead oxide, stilbene is formed:



Very probably an intermediate compound is formed at first which afterwards loses a molecule of water:

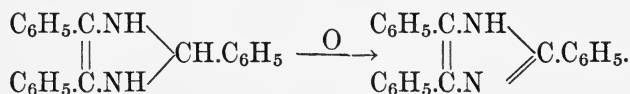


The hydrogen addition products of the aromatic hydrocarbons can also lose their hydrogen by the action of oxidants, like fuming nitric acid, for instance, only, in place of obtaining the aromatic hydrocarbon, the nitro derivatives are produced: thus,  $\text{C}_6\text{H}_4(\text{CH}_3)_2.\text{H}_6$ , hexahydride of xylene, gives  $\text{C}_6\text{H}(\text{NO}_2)_3.(\text{CH}_3)_2$ .

In the same manner the hydro-pyridine compounds lose hydrogen and pass into the pyridine derivatives. For example, piperidine,  $\text{C}_5\text{H}_{11}\text{N}$ , gives pyridine,  $\text{C}_5\text{H}_5\text{N}$ ; the hydrochloride of conicine,  $\text{C}_8\text{H}_{17}\text{NC}_5\text{H}_4(\text{C}_3\text{H}_7)\text{N}.\text{H}_6$ , gives propylpyridine,  $\text{C}_5\text{H}_4(\text{C}_3\text{H}_7)\text{N}$ .

The removal of hydrogen from nitrogen compounds by oxi-

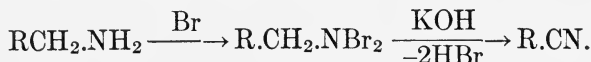
dation gives rise to a double linking between two carbon atoms, between a carbon and a nitrogen atom, or between two nitrogen atoms.<sup>1</sup> Thus, amarine,  $C_{21}H_{18}N_2$ , gives lophine,  $C_{21}H_{16}N_2$ , on oxidation with an acetic acid solution of chromic acid. These two bodies can be represented by the following formulas:



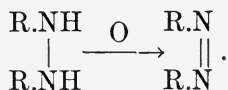
The primary amines of the paraffin series, on oxidation with an alkaline solution of bromine, yield nitriles:



These latter bodies may be converted again into amines by reducing agents. Without doubt, the removal of hydrogen from the amines takes place through the formation of an intermediate derivative,  $\text{R.CH}_2.\text{NBr}_2$ , which subsequently, by the action of the alkali, splits off  $2\text{HBr}$ :



The hydrazo derivatives are easily changed into azo-compounds:



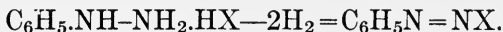

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<sup>1</sup> The oxidizing action of the air converts para-phenylene-diamine,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{NH}_2 \\ \text{NH}_2 \end{smallmatrix}$ , into tetra-amido-diphenyl-para-azophenylene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{N} & \text{N} \\ | & | \\ \text{N} & \text{N} \end{smallmatrix} \begin{smallmatrix} \text{C}_6\text{H}_3 & \text{C}_6\text{H}_3 \\ \text{NH}_2 & \text{NH}_2 \\ \text{NH}_2 & \text{NH}_2 \end{smallmatrix}$ .

Manganese dioxide and sulphuric acid, however, convert it into quinone, while, with bleaching-powder, it gives quinone-dichloride; para-amidophenol is also oxidized in dilute solution by the air.

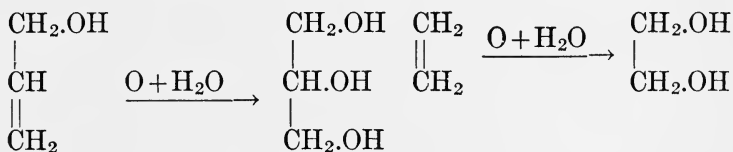
This may be brought about by the action of nitrous acid, mercury oxide, chlorine, bromine, ferric chloride, Fehling's solution, etc. In many cases simply atmospheric oxygen is sufficient.

The hydrazines also give diazo derivatives; thus, the salts of phenyl-hydrazine, with mercuric oxide, are changed into the salts of diazo-benzene:



In some cases, oxidation is accompanied by a hydration, especially with unsaturated compounds. One would think that in most cases the action of oxidizing agents in such bodies would be to break up the double-linking; but from recent researches (principally those of Wagner) it would seem that these bodies, when oxidized by potassium permanganate, preserve the integrity of their molecule, and that the rupture is only due to the oxidation which is continued on the bodies formed in the first place. According to this, there would occur in unsaturated compounds the fixation of  $\text{O} + \text{H}_2\text{O}$ , that is to say, the elements of hydrogen dioxide, or  $2(\text{OH})$ .<sup>1</sup>

It is in this manner that the unsaturated hydrocarbons  $\text{C}_n\text{H}_{2n}$  are transformed into glycols, and the unsaturated alcohols  $\text{C}_n\text{H}_{2n}\text{O}$  into glycerols:



The yield of glycol is about 50 per cent. of the theoretic quantity; it may be increased by taking a weaker oxidant. This is the simplest manner of obtaining the higher glycols.

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<sup>1</sup> See Wagner, *Action of Oxidants*, etc. This kind of reaction is very similar to that of A. Zaytzeff, who admits the formation of an oxide and the subsequent fixation of a molecule of water. It is known, besides, the oxygenated water  $(\text{OH})_2$  combines directly with ethylene, giving ethylenic glycol.

In the researches of Wagner, the method of procedure was as follows: 30 grams of the hydrocarbon are placed in a large flask with a litre of water, and vigorously agitated, while adding about 5 litres of a 1 per cent. solution of potassium permanganate. The proportions should be such that there is 1 atom of oxygen for 1 molecule of the hydrocarbon, and 1.5 to 2 atoms for higher numbers.

The action of potassium permanganate on the hydrocarbons  $C_nH_{2n}$  furnishes a good means of establishing their constitution.

The oxidation of the alcohols  $C_nH_{2n}O$  with potassium permanganate gives trihydric alcohols. The hydrocarbons, with two double bonds  $C_nH_{2n-2}$ , as, for instance, diallyl, are converted into tetrahydric alcohols by reason of the fixation of  $O_2 + 2H_2O = (OH)_4$ .

The unsaturated hydrocarbons and acids are easily changed into saturated acids by the action of potassium permanganate. A. Zaytzeff<sup>1</sup> has shown that oleic acid,  $C_{18}H_{34}O_2$ , is transformed into dioxy-stearic acid,  $C_{18}H_{34}(OH)_2O_2$ .<sup>2</sup> From fumaric acid in the same manner is prepared tartaric acid.<sup>3</sup>

The supposition may be made that in this transformation of unsaturated acids into saturated ones, for example, of palmitic acid  $C_{16}H_{32}O_2$  into oxy-palmitic acid,  $C_{16}H_{32}O_4$ , there is not a fixation of  $O_2$ , but a combination with  $(OH)_4$ , accompanied by a liberation of  $2H_2O$ .

Wagner thus gives an explanation of the interesting fact of the change of non-symmetrical ethylene dibromide into brom-acetyl-bromide  $CH_2Br.CO.Br$ , observed by Demole.

<sup>1</sup> *Jour. Soc. Phys. Chim. Russe*, vol. 17, p. 417.

<sup>2</sup> *Ibid.*, vol. 24, pp. 13-27.

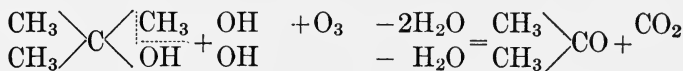
<sup>3</sup> S. Tanatar, *On the Constitutional Formulae of Fumaric and Oleic Acids*. See *Jour. Soc. Phys. Chim. Russe*, vol. 13 (2), p. 256.

### B. Direct Oxidation Accompanied by Decomposition of the Molecule.

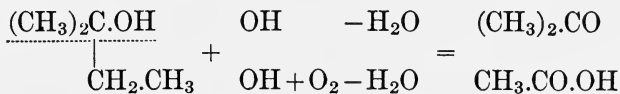
This series of reactions includes the influence of oxidants on tertiary alcohols, polyhydric alcohols,<sup>1</sup> ketones, and many aromatic compounds.

The oxidation of tertiary alcohols takes place with fixation of  $O + H_2O$ ; the two groups which are the richest in hydrogen remain in combination with the  $C.OH$  group, while the third radical is split off and is subjected to a further oxidation.

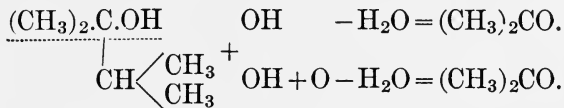
Thus, in the oxidation of trimethyl-carbinol there is obtained acetone and carbon dioxide:



Dimethyl-ethyl-carbinol, under the same conditions, gives acetone and acetic acid:



with isopropyl-dimethyl-carbinol; two molecules of acetone are obtained:

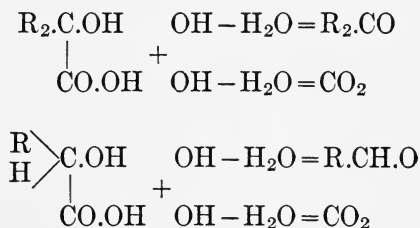


The acid-alcohols behave in the same manner as the tertiary alcohols.

Thus, with the tertiary acid-alcohol,  $R_2C \begin{array}{c} \text{OH} \\ \text{COOH} \end{array}$ , the ketone

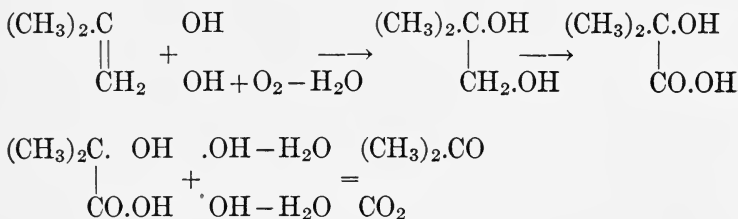
<sup>1</sup> Prjibuitek, *On Some Oxidation Products of the Polyatomic Alcohols*. St. Petersburg, 1881 (in Russian). By the oxidation of erythrite with potassium permanganate, oxalic acid was obtained.

$R_2CO$  is formed; with the secondary acid-alcohol  $RCH\begin{matrix} \nearrow OH \\ \searrow COOH \end{matrix}$ , the aldehyde  $R.CHO$  is formed:



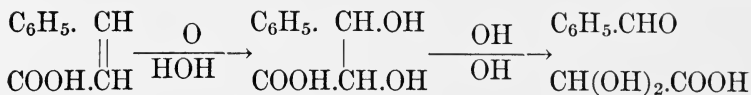
Certain acids of the preceding general formula are sometimes oxidized and still preserve the integrity of their molecule.

The decomposition of the unsaturated hydrocarbons by the action of oxidants is merely the result of a further oxidation of the first products formed. By fusing with caustic potash, for instance, some of the acids of the acrylic series undergo an oxidation simultaneous with their reduction. Also, isobutylene on oxidation gives a glycol, which further yields an hydroxy-acid, and the latter is decomposed into a ketone and an acid:

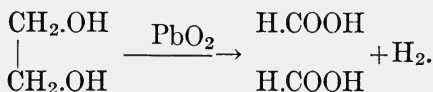


If the oxidation takes place in the presence of an acid, a glycol is formed, which then loses a molecule of water, and by a further oxidation gives abnormal products.

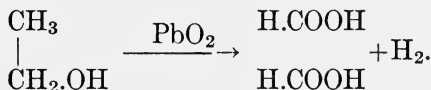
Cinnamic acid,  $C_6H_5.CH:CH.COOH$ , for example, should give at first, on oxidation, a di-acid alcohol, and this latter body is subsequently converted into benzaldehyde and glyoxylic acid:



These finally are converted by oxidation into benzoic acid and oxalic acid. These reactions serve as a means of detecting the presence of cinnamic acid, it being recognized by evolving the odor of benzaldehyde when heated with  $\text{PbO}_2$ . It might be noted that this method of oxidation frequently causes a division of the molecule.<sup>1</sup> Glycol, for instance, in dilute alkaline solution, when treated with lead peroxide, gives formic acid with a simultaneous evolution of hydrogen gas:



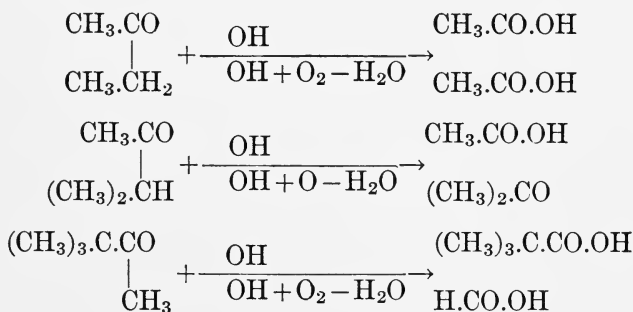
Alcohol, cane-sugar, and other such compounds behave in a similar manner, yielding the same products:



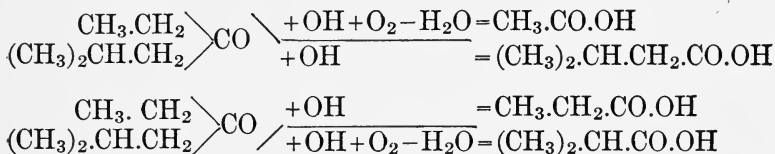
Ortho-nitrobenzaldehyde may be conveniently prepared from cinnamic acid. The solution of the latter is poured into benzene, and there is added with constant stirring a dilute solution of potassium permanganate. The aldehyde at first formed passes into solution in the benzene, and is thus preserved from further oxidation. This, in fact, is a good general method for protecting easily oxidizable products from being decomposed by successive oxidation. After each addition of the oxidant, the liquid should be well shaken or stirred, in order to remove the aldehyde as much as possible from the further oxidizing influence of the potassium permanganate.

<sup>1</sup> Thus uric acid gives allantoin.

Ketones are oxidized with hydrolysis; that is to say, there is a fixation of  $O + H_2O = (OH)_2$ . For example:



The oxidation of ketones is a more complicated reaction than would at first sight appear.<sup>1</sup> In fact, the products which are obtained are dependent upon the nature of the oxidant and the circumstances of the reaction. Thus, with chromic acid mixture, there is usually obtained, not two, but four, compounds; the decomposition taking place in two different directions, on account of the oxidation of the two  $\text{CH}_3$  groups attached to the  $\text{CO}$ . We have a proof of it in the oxidation of ethyl-isobutyl-ketone: the principal products formed are acetic and isovaleric acids, while, at the same time, propionic and isobutyric acids are produced:



One form of the decomposition always predominates over the other. That found in the example given above is exactly contrary to the ideas of Popoff. In some ketones, where the

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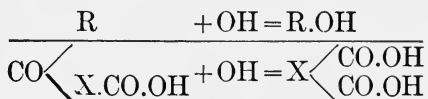
<sup>1</sup> More so than is included in Popoff's law of oxidation. See A. Popoff, *On the Oxidation of Ketones*, Kazan, 1869; and *On the Normal Oxidation of Ketones*, Warsaw, 1877. See also Wagner, *Synthesis and Oxidation of the Secondary Alcohols*, St. Petersburg, 1885. (All of these in Russian.)



two atoms of carbon linked to the CO group do not have hydrogen, oxidation takes place without rupture of the molecule, and with the formation of a ketonic acid,  $C_6H_5.CO.C_6H_4.CH_3$ , is oxidized to  $C_6H_5.CO.C_6H_4.CO.OH$ .

The temperature has an influence on the character of the reaction. In the cold, methyl-butyl-ketone with potassium permanganate, or chromic acid, gives only butyric and acetic acids; if heat is employed, there is formed an acid containing more carbon atoms (probably valeric acid).

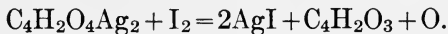
Similarly to the ketones, the ketonic acids are decomposed according to the following reaction:



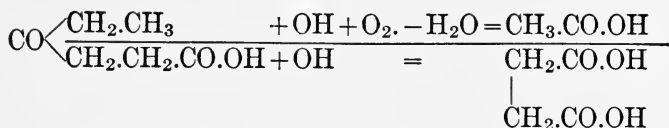
The group  $R.OH$  then undergoes a further oxidation. The higher fatty acids are decomposed by oxidation into mono- and di-carboxylic acids, with the constant and characteristic formation of succinic acid. The silver salts of the fatty acids are partially decomposed on dry distillation; this decomposition may be represented by the equation:



The salts of diatomic acids, such as fumaric acid, are entirely decomposed by iodine. The oxygen liberated oxidizes the anhydride found in accordance with the equation:

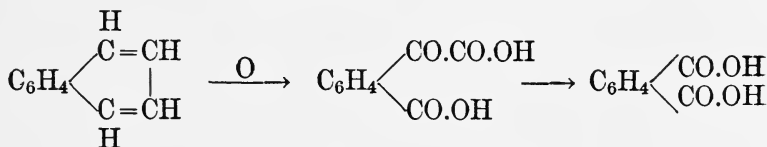


Caproic acid,  $CH_3.CH_2.CH_2.CH_2.CH_2.CO.OH$ , with nitric acid, gives acetic and succinic acids; from cenanthylic acid,  $CH_3.-CH_2.CH_2.CH_2.CH_2.CH_2.CO.OH$ , propionic and succinic acids are obtained. It is probable that ketonic acids are formed, which are further decomposed according to the equation:



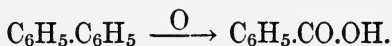
It is possible that the decomposition of different aromatic hydrocarbons by oxidation may proceed with the formation of ketones. All that is known is, that the oxidation of ethyl benzene,  $\text{C}_6\text{H}_5.\text{CH}_2.\text{CH}_3$ , gives the ketone  $\text{C}_6\text{H}_5.\text{CO}.\text{CH}_3$ , acetophenone.

The oxidation of naphthalene into phthalic acid, as experience proves, does not take place directly, but a ketonic acid is formed as an intermediate product:



The best oxidant to employ is a chromic acid mixture: the acetic acid solution of chromic acid gives principally the naphthoquinone  $\text{C}_{10}\text{H}_6\text{O}_2$ . Quinoline,  $\text{C}_4\text{H}_4.\text{C}_5\text{H}_3\text{N}$ , behaves like naphthalene and gives pyridine dicarboxylic acid  $(\text{COOH})_2.\text{C}_5\text{H}_3\text{N}$ .

It has been shown that in the oxidation of aromatic hydrocarbons, the groups  $\text{C}_n\text{H}_{2n+1}$ , like  $\text{CH}_3$ , are converted into carboxyl,  $\text{COOH}$ ; the group  $\text{C}_6\text{H}_5$  behaves in a like manner, and thus diphenyl gives benzoic acid:



The oxidation of additive hydrogen aromatic compounds gives some interesting results: quinic acid,  $\text{C}_6\text{H}_7(\text{OH})_4\text{CO.OH}$ , with manganese dioxide and sulphuric acid, is converted into qui-

none; it was in this manner that the latter was discovered by Woskresenky.<sup>1</sup> The hydrochloride of  $\alpha$ -tetra-hydro-naphthylamine,  $\text{NH}_2\cdot\text{C}_{10}\text{H}_7\cdot\text{H}_4$ , with permanganate, gives adipic acid,  $\text{C}_6\text{H}_{10}\text{O}_4$  (yield, about 18 per cent).

Benzene with potassium chlorate and sulphuric acid gives  $\beta$ -trichlor-acetyl-acrylic acid,  $\text{CCl}_3\cdot\text{CO}\cdot\text{CH}=\text{CH}\cdot\text{CO}\cdot\text{OH}$  (also called trichlor-phenomalic acid), which has been wrongly taken for trichlor-hydroquinone.

The azo derivatives are oxidized with a decomposition of their molecule. It is probable that azo-benzene,  $\text{C}_6\text{H}_5\text{N}:\text{N}\cdot\text{C}_6\text{H}_5$ ,<sup>2</sup> heated for some time in a sealed tube with an acetic acid solution of chromic acid, is converted into nitrobenzene,  $\text{C}_6\text{H}_5\cdot\text{NO}_2$ (?).<sup>3</sup>

#### IV. INDIRECT OXIDATION.

##### A. Substitution of a Halogen by the Hydroxyl Group.<sup>4</sup>

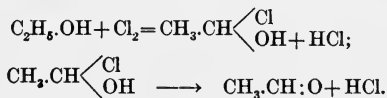
This reaction, which results in the formation of an alcohol, may be brought about by the action of water alone; generally it is necessary to heat in a sealed tube. If the alcohol formed is soluble in water, it may be isolated by means of potassium carbonate. Tertiary compounds more easily give up the halogen than do the secondary compounds; and these, in turn, more readily than the primary compounds.

<sup>1</sup> A. Woskresensky, *On Quinic Acid and the Discovery of a New Product, Quinone*, St. Petersburg, 1839 (in Russian).

<sup>2</sup> Pétrieff, *Data for the Study of Azo-Benzene*, Odessa, 1872 (in Russian).

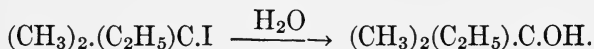
<sup>3</sup> See *Jour. Soc. phys. Chim. Russe*, vol. 18, p. 387.

<sup>4</sup> The conversion of primary alcohols into aldehydes by the oxidizing action of chlorine is no doubt an indirect reaction, there first being a substitution of hydrogen by chlorine and then a subsequent splitting off of hydrochloric acid:



The formation of chloral from ethyl alcohol may be explained in this way, there also occurring a simultaneous substitution of the hydrogen of the  $\text{CH}_3$  group by chlorine.

For example, tertiary amyl iodide is easily converted into the corresponding alcohol by agitation with cold water:



Triphenyl-brom-methane,  $(\text{C}_6\text{H}_5)_3\text{C.Br}$ , behaves in the same manner. Isopropyl iodide,  $(\text{CH}_3)_2\text{CHI}$ , however, is only converted into isopropyl alcohol,  $(\text{CH}_3)_2\text{CH.OH}$ , after a long heating under pressure with a large quantity of water. And the conversion of isobutyl iodide  $(\text{CH}_3)_2\text{CH.CH}_2\text{I}$ , or of primary isoamyl chloride  $(\text{CH}_3)_2\text{CH.CH}_2\text{CH}_2\text{Cl}$ , takes place with even greater difficulty. Isobutyl iodide, however, with silver oxide and water, instead of giving the corresponding alcohol, gives tertiary butyl alcohol.

This method of obtaining alcohols is only applicable in cases where the halogen compound does not easily form an unsaturated body through the splitting off of hydrochloric acid. In all cases, however, it is best to use an excess of water in order to prevent the formation of an unsaturated body. For instance,  $\alpha$ -hexyl iodide with a small amount of water gives hexylene and hydriodic acid; with a large excess of water, it furnishes the alcohol,  $\text{CH}_3(\text{CH}_2)_3\text{CH}(\text{OH})\text{CH}_3$ . Sometimes, secondary products are formed; on heating ethyl bromide with a little water to  $200^\circ \text{C}$ ., ethyl oxide is formed, at the same time as ethylene,  $\text{C}_2\text{H}_4$ , and hydrobromic acid, from the further action of the ethyl bromide on the alcohol.

In decomposing the iodides, sealed tubes may be avoided by the use of oxides ( $\text{PbO}$ ,  $\text{Ag}_2\text{O}$ ,  $\text{HgO}$ ), barium hydrate ( $\text{Ba}(\text{OH})_2$ ), or the carbonated alkalies,  $\text{K}_2\text{CO}_3$  and  $\text{Na}_2\text{CO}_3$ . Silver oxide is particularly good for those iodides which easily give unsaturated compounds, for the reaction then takes place without the necessity of heating. The other hydrates and carbonates only act well on boiling, and always lead to the formation of unsaturated compounds. In certain cases, when these latter cannot be formed, the substitution of a halogen by OH is effected by the aid of the hydrates of the alkaline metals.

Thus, monochloroacetic acid,  $\text{CH}_2\text{ClCOOH}$ , with potassium hydrate, is converted into glycollic acid,  $\text{CH}_2\text{OHCOOH}$ .

If there are several halogen atoms present in the molecule, they are usually all replaced together, whether they are fixed to a single carbon atom or to several carbon atoms. Thus, benzylidene chloride,  $\text{C}_6\text{H}_5\text{CHCl}_2$ , gives benzaldehyde,  $\text{C}_6\text{H}_5\text{CHO}$  (the best process is to heat with anhydrous oxalic acid). The  $\alpha$ -dichloropropionic acid behaves in the same manner. Phenylchloroform,  $\text{C}_6\text{H}_5\text{CCl}_3$ , with water at  $150^\circ \text{C}$ ., very readily yields benzoic acid,  $\text{C}_6\text{H}_5\text{COOH}$ ; and the action of soda on the ether of trichlorolactic acid,  $\text{CCl}_3\text{CH(OH)COOH}$ , is the most convenient method for the preparation of tartronic acid,  $\text{CH(OH)(COOH)}_2$ . In the same way, ethylene chloride,  $\text{CH}_2\text{ClCH}_2\text{Cl}$ ,

$\text{CH}_2\text{ClCH}_2\text{Cl}$ , gives glycol, and trichlorohydrin,  $\text{CH}_2\text{ClCHClCH}_2\text{Cl}$ , with 20 parts of water at  $160^\circ \text{C}$ ., gives glycerol. Occasionally, however, when  $\text{C}_n\text{H}_{2n}\text{Br}_2$  is heated with water, instead of obtaining the corresponding glycol, an aldehyde or a ketone is produced. Sometimes all of the halogens cannot be removed; dibromopropionic acid,  $\text{CH}_2\text{BrCHBrCOOH}$ , on boiling with water and silver oxide, is only converted into bromhydracrylic acid,  $\text{CH}_2\text{(OH)CHBrCOOH}$ .

For the preparation of glycols, especially the lower homologues, the halogen compound may be boiled with a large excess of water, and the theoretic quantity of carbonate of potash with an inverted condenser. With water alone, the reaction proceeds slowly, and only when heated under pressure. The yield is increased with the quantity of water, but it is difficult to obtain 50 per cent. of the theoretical amount, as there is always a part of the compound which is changed into an unsaturated body.

The introduction of OH can be made in a simple manner by the action of a silver salt (or of another metal) on any of

the acids; in this manner an ester is at first obtained which is subsequently saponified.

During the replacement of a halogen by OH in the substituted carboxylic acids, hydrochloric acid is often evolved. The best results are obtained by a long-continued heating with water alone.

When the halogen occurs in the benzene ring, in order to replace it with OH, it is necessary to fuse with potash. Mono-iodo-benzene, however, by this method does not give a trace of phenol.

The displacement occurs more readily if the compound contains, next to the halogen atom, another halogen atom, or one of the groups OH, NO<sub>2</sub>, or COOH. Thus, dibrom-toluene,

$\text{C}_6\text{H}_3 \begin{matrix} \swarrow (1) \text{CH}_3 \\ (3) \text{Br} \\ \searrow (5) \text{Br} \end{matrix}$  with a little water in a sealed tube, gives orcinol,

$\text{C}_6\text{H}_3 \begin{matrix} \swarrow (1) \text{CH}_3 \\ (3) \text{OH} \\ \searrow (5) \text{OH} \end{matrix}$ . Ortho-iodo-phenol,  $\text{C}_6\text{H}_4 \begin{matrix} \swarrow (1) \text{I} \\ (2) \text{OH} \end{matrix}$ , on fusion

with potash, gives pyrocatechol,  $\text{C}_6\text{H}_4 \begin{matrix} \swarrow (1) \text{OH} \\ (2) \text{OH} \end{matrix}$ , and meta-chlor-benzoic acid gives meta-oxy-benzoic acid. Hexachlor-benzene,  $\text{C}_6\text{Cl}_6$ , heated with glycerol and caustic soda, is converted into  $\text{C}_6\text{Cl}_5\text{OH}$ . and, with water at 200° C., into  $\text{C}_6\text{H}_4 \begin{matrix} \swarrow (1) \text{OH} \\ (2) \text{OH} \end{matrix}$ , pyrocatechol.

It often happens in these fusions with potash that there is a molecular transformation, either by reason of too prolonged an action or too high a temperature. The ortho- and meta-bromphenols, when fused with potash, both give pyrocatechol and resorcinol,  $\text{C}_6\text{H}_4 \begin{matrix} \swarrow (1) \text{OH} \\ (3) \text{OH} \end{matrix}$ . The alkali during the fusion behaves at times as a reducing agent and again as an oxidant; and thus it is possible to explain the molecular transposition by two successive reactions of oxidation and reduction. The ortho-bromphenol,  $\text{C}_6\text{H}_4 \begin{matrix} \swarrow (1) \text{OH} \\ (2) \text{Br} \end{matrix}$ , is at first transformed into

$C_6H_3$   $\begin{matrix} \swarrow (1) \text{ OH} \\ \leftarrow (2) \text{ Br} \\ \searrow (3) \text{ OH} \end{matrix}$ , and then into resorcinol,  $C_6H_4$   $\begin{matrix} \swarrow (1) \text{ OH} \\ \leftarrow (3) \text{ OH} \end{matrix}$ .

The presence of the  $NO_2$  group facilitates the exchange of halogens with OH, especially when the two substituents are in the ortho (1:2) or meta (1:3) positions. In the latter case the influence is so great that the nitro-chlor-benzene,  $C_6H_4$   $\begin{matrix} \swarrow (1) \text{ Cl} \\ \leftarrow (2) \text{ NO}_2 \end{matrix}$ , may be transformed into ortho-nitrophenol,  $C_6H_4$   $\begin{matrix} \swarrow (1) \text{ OH} \\ \leftarrow (2) \text{ NO}_2 \end{matrix}$ , by gently heating with an alkali. If there are two nitro groups, boiling with sodium carbonate is sufficient to replace a halogen with the OH group; as, for example, with dichlor-dinitro-

benzene,  $C_6H_2$   $\begin{matrix} \swarrow (1) \text{ Cl} \\ \leftarrow (2) \text{ NO}_2 \\ \leftarrow (4) \text{ Cl} \\ \searrow (6) \text{ NO}_2 \end{matrix}$ , which, under the conditions men-

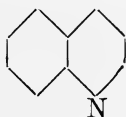
tioned, gives chlor-dinitro-phenol:  $C_6H_2$   $\begin{matrix} \swarrow (1) \text{ OH} \\ \leftarrow (2) \text{ NO}_2 \\ \leftarrow (4) \text{ Cl} \\ \searrow (6) \text{ NO}_2 \end{matrix}$ . It may

happen with chlor-nitro-compounds, if there are several  $NO_2$  groups, that one of these may also be exchanged for OH.

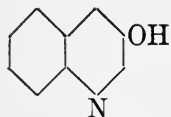
Among the other aromatic compounds, which readily exchange their halogen groups for others, are to be noticed the brom-anthraquinones, and the halogen derivatives of quinoline (in the pyridine nucleus). Thus, mono-brom-anthraquinone,

$C_6H_4$   $\begin{matrix} \swarrow \text{CO} \\ \leftarrow \text{CO} \end{matrix}$   $C_6H_3Br$ , on fusion with potash at a moderate temperature, gives monoxo-anthraquinone,  $C_6H_4$   $\begin{matrix} \swarrow \text{CO} \\ \leftarrow \text{CO} \end{matrix}$   $C_6H_3OH$ .

The oxidation is the more complete as the temperature is more

elevated. The  $\alpha$ -chlor-quinoline, , is distinguished

from its isomers in that, when heated with water at  $120^\circ C.$ , it gives

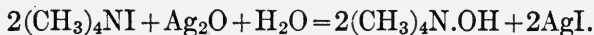


; while the  $\beta$ - and  $\gamma$ -chlor-quinolines undergo no change even when heated with potash at  $220^{\circ}$  C.

The chlorides of the organic acids, such as benzoyl chloride,  $\text{C}_6\text{H}_5\cdot\text{CO}\cdot\text{Cl}$ , and acetyl chloride,  $\text{CH}_3\cdot\text{CO}\cdot\text{Cl}$ , readily exchange their Cl for OH by the action of water.

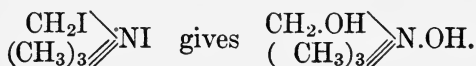
The chlorides of the sulphonic acids are very stable in their behaviour, and in order to transform them into their corresponding acids it is necessary to subject them to prolonged boiling with water, or, in order to accelerate the reaction, with metallic hydrates or oxides.

In compounds analogous to  $(\text{CH}_3)\text{SI}$ , the halogen may be replaced by OH with the aid of recently prepared hydrated oxide of silver. Halogens united to nitrogen behave in the same manner:



The chlorine derivatives of amines are not as readily decomposed as the iodine compounds. Thus:  $\text{N}(\text{Cl}) \begin{cases} \text{CH}_2\cdot\text{C}_6\text{H}_5 \\ \text{C}_6\text{H}_5 \\ \text{(CH}_3)_2 \end{cases}$

(formed by the action of benzyl chloride on dimethylaniline) is not at all converted into the corresponding hydrate by the action of moist silver oxide. In this particular case it is necessary to prepare the sulphonic derivative, which is then decomposed with the theoretical amount of baryta. In a salt of an amine, when a halogen is united to carbon, it may be replaced by OH by the aid of moist silver oxide, or may even be eliminated in the form of its hydrogen acid:

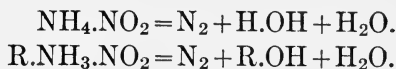




## B. Oxidation by the Use of Ammonia Derivatives.

The displacement of  $\text{NH}_2$  by  $\text{OH}$  (from bases or from acids) is brought about by the action of nitrous acid.

The nitrites of the amines behave like the nitrite of ammonia when heated with water:



In order to transform  $\text{NH}_2$  into  $\text{OH}$ , the nitrite of the amine is first prepared (by double decomposition of the hydrochloride with silver nitrite,  $\text{AgNO}_2$ ), then subsequently decomposed by heat; or, further, by treating the amine with nitrous oxide,  $\text{N}_2\text{O}_3$ , in the presence of water, until nitrogen ceases to be evolved.

The amines of the paraffin series often give secondary products. Thus, normal butyl-amine,  $\text{C}_3\text{H}_7.\text{CH}_2.\text{NH}_2$ , besides normal butyl alcohol,  $\text{C}_3\text{H}_7.\text{CH}_2.\text{OH}$ , also gives secondary butyl alcohol,  $\text{CH}_3.\text{CH}_2.\text{CH} \begin{smallmatrix} \text{CH}_3 \\ \text{OH} \end{smallmatrix}$ , butylene,  $\text{CH}_3.\text{CH}_2.\text{CH}=\text{CH}_2$ , and  $(\text{C}_4\text{H}_9)_2.\text{N.NO}$ .

In the benzene derivatives the reaction is brought about by heating any salt of the azo compounds with water.

A good yield of meta-chlor-phenol (1:3) may be obtained in the following manner: Dissolve in water the nitrate of meta-chlor-aniline,  $\text{C}_6\text{H}_4 \begin{smallmatrix} (1) \text{NH}_2.\text{HNO}_3 \\ (3) \text{Cl} \end{smallmatrix}$ , cool well, and saturate with a current of  $\text{N}_2\text{O}_3$  gas; on adding a cold concentrated solution of mercuric chloride,  $\text{HgCl}_2$ , a double compound of mercury separates out, which is subsequently decomposed by boiling with water until nitrogen ceases to be evolved. Soda is added; the oxide of mercury is filtered off; the filtrate is acidulated, and the chlor-phenol is separated by dissolving in ether.

The same method of making phenols may also be used in the preparation of oxy-phenols, the chlor- and nitro-derivatives,

the oxy-aldehydes, oxy-ketones. Certain of the brom- and chlor-amines present exceptions to the usual procedure, the  $\text{NH}_2$  being replaced by H instead of OH. Thus, the diazo-

compound of dibrom-aniline,  $\text{C}_6\text{H}_3 \begin{smallmatrix} \swarrow (2) \text{ Br} \\ (1) \text{ NH}_2 \\ \searrow (4) \text{ Br} \end{smallmatrix}$ , when decom-

posed by boiling with water, gives di-brom-benzene; the

chlor-toluidine,  $\text{C}_6\text{H}_3 \begin{smallmatrix} \swarrow (1) \text{ CH}_3 \\ (3) \text{ Cl} \\ \searrow (4) \text{ NH}_2 \end{smallmatrix}$ , in place of chlor-cresol gives

chlor-toluene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{ CH}_3 \\ (3) \text{ Cl} \end{smallmatrix}$ .

The  $\text{NH}_2$  group in acid amides of amido-carboxyl and amido-sulphonic acids is very resistant to the action of nitrous acid,  $\text{N}_2\text{O}_3$ .<sup>1</sup> Thus, the amides of the meta- and para-amido-

benzoic acids,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow \text{NH}_2 \\ \searrow \text{CO.NH}_2 \end{smallmatrix}$ , through the medium of the

diazo reaction, are converted into  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow \text{OH} \\ \searrow \text{CO.NH}_2 \end{smallmatrix}$ , but the group  $\text{CO.NH}_2$  remains unchanged; the amide of the ortho-amido-

sulphonic acid of benzene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{ NH}_2 \\ \searrow (2) \text{ SO}_2\text{NH}_2 \end{smallmatrix}$ , behaves in the same way.

If a very negative element or radical occurs with the  $\text{NH}_2$  group, the latter, by the action of alkalis, is often converted into OH with the elimination of ammonia. Many aromatic amido compounds in which the  $\text{NH}_2$  is in the ortho- or para-position to  $\text{NO}_2$  behave in this manner. For example, para-

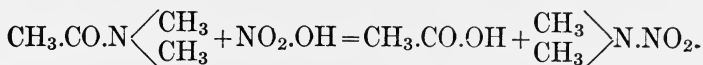
nitro-aniline,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{ NH}_2 \\ \searrow (4) \text{ NO}_2 \end{smallmatrix}$ , with potash, gives para-nitro-

phenol,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{ OH} \\ \searrow (4) \text{ NO}_2 \end{smallmatrix}$ .

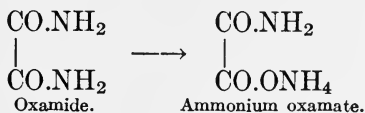
<sup>1</sup> If there is no  $\text{NH}_2$  group in the aromatic nucleus, then it is the  $\text{SO}_2\text{NH}_2$  group which is attacked by the nitrous oxide. Thus:



The  $\text{NH}_2$  group when joined to  $\text{CO}$ , is easily converted into  $\text{OH}$  by the action of acids or alkalies. The acid amides are thus changed into carboxylic acids. Formamide with concentrated caustic potash, even in the cold, gives potassium formate with liberation of  $\text{NH}_3$ . In other cases it is necessary to boil with the alkali for a prolonged time in order to liberate all of the ammonia. In place of potash, soda may be used, or even barytes or caustic lime. The  $\text{NH}_2$  group in acid amides is converted into  $\text{OH}$  by the action of nitric acid. Thus,  $\text{CH}_3.\text{CO}.\text{NH}_2 + \text{NO}_2.\text{OH} = \text{CH}_3.\text{CO}.\text{OH} + \text{N}_2\text{O} + \text{H}_2\text{O}$ . Substituted acid amides, such as methyl-acetamide, behave in the same manner. By the action of nitric acid on dimethyl-acetamide, there is formed, at the same time with the acetic acid, dimethylnitramine:



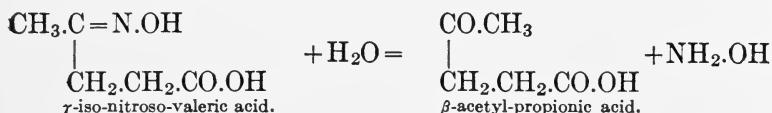
The amides of the di-acids, by the action of boiling ammonia, are converted into the amido-ammonium salts. For example:



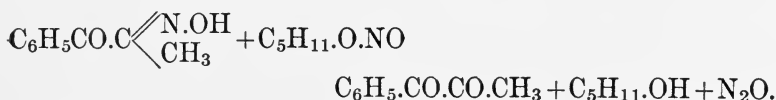
If alkalies act but slowly on acid amides, they may be heated in a sealed tube with concentrated hydrochloric acid. With the keto-amides  $\text{R}.\text{CO}.\text{CO}.\text{NH}_2$ , however, it is necessary to operate with caution, for they are easily decomposed:  $(\text{CH}_3)_2.\text{CH}.\text{CO}.\text{CO}.\text{NH}_2$ , by the moderate action of hydrochloric acid, furnishes, simultaneously with the acid,  $(\text{CH}_3)_2.\text{CH}.\text{CO}.\text{CO}.\text{OH}$ , considerable iso-butyric acid,  $(\text{CH}_3)_2.\text{CH}.\text{COOH}$ .

The amides of sulphonic acids, on treatment with hydrochloric acid at  $150^\circ \text{C}$ ., are converted into sulphonic acids; if the reaction is energetic it may even happen that the  $\text{SO}_2.\text{OH}$  group is removed. The  $\text{SO}_2.\text{NH}_2$  group is very resistant to alkalies.

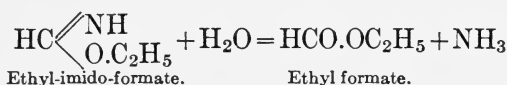
The transformation of  $>\text{N.OH}$  into  $\text{O}$  takes place by the action of concentrated hydrochloric acid on the iso-nitroso-compounds and aldoximes, heating if necessary; a weaker acid, such as acetic, may also be used:



Iso-nitroso bodies are decomposed in the same manner by the action of amyl nitrite:



The transformation of  $>\text{NH}$  into  $\text{O}$  takes place sometimes by the action of water at ordinary temperatures, and also on heating with dilute acid. The imido-ethers (action of alcohols on nitriles) are decomposed very easily:



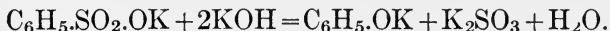
The nitriles may be converted into esters of the acids through the means of imido-ethers. Benzoyl-formic ester is easily prepared by passing hydrochloric acid into a cold solution of benzoyl cyanide,  $\text{C}_6\text{H}_5.\text{CO.CN}$ , in alcohol. The liquid is allowed to stand for several days, and the ester is separated with water. The conversion of guanidine into urea by the action of boiling baryta-water is another example of the change of  $\text{NH}$  into  $\text{O}$ .

The transformation of  $\text{N}=\text{N}$  into  $\text{H}$  and  $\text{OH}$  is brought about by prolonged boiling with water of the esters of the diazo acids

of the paraffin series. The ester of diazo-acetic acid,  $\text{HC} \begin{array}{l} \diagup \text{N} \\ \diagdown \parallel \\ \text{N} \end{array}$ ,  
 $\text{CO}_2.\text{C}_2\text{H}_5$ ,  
 gives the ester of glycollic acid.

### C. Conversion of the Sulphonic Acid Group into the Hydroxyl Group.<sup>1</sup>

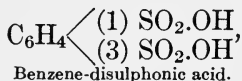
This reaction, which is often employed in the aromatic series, is brought about by the fusion of the sulphonic acids with caustic potash, followed by decomposition by an acid:



The sulphonic acid is heated in a silver or nickel crucible by vapor of naphthalene or anthracene with solid caustic potash to which is added a little water. The time of the fusion varies from several minutes to several hours, and the temperature varies from 160° to 300° C. The yield of the phenol increases with the temperature and the amount of alkali. With 6 molecules of KOH on  $\text{C}_6\text{H}_5.\text{SO}_2.\text{OK}$  and heating for 1 hour, a yield of 94 per cent. of the theoretical may be obtained. The exact time of stopping the fusion cannot always be easily recognized. When the reaction is finished, the mass is broken up and dissolved in water and acidulated; if nothing separates out, extract with ether.

Instead of using the free sulphonic acid, the lead salt may be employed, which is often prepared in order to purify the acid. When an aromatic body is fused with potash in the presence of an oxidizing body, there may occur the oxidation of a hydrogen in the nucleus. In this manner the hydroxy-anthraquinones (alizarins) may be prepared.

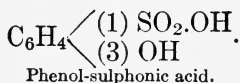
If there are two sulphonic acid groups in the same molecule, by using suitable precautions a single one may be substituted; if the reaction is very energetic, both will be attacked:



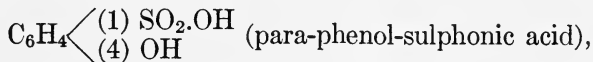

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<sup>1</sup> This is equivalent to the replacement of H by OH through the medium of the sulphonic acid derivatives.

at 170–180° C., is converted into



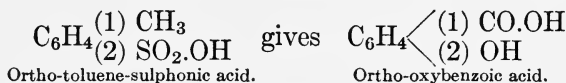
Frequently fusions with potash lead to molecular transpositions. With the acid



resorcinol,  $\text{C}_6\text{H}_4 \begin{matrix} \swarrow (1) \text{OH} \\ \searrow (3) \text{OH} \end{matrix}$ , is obtained, which is a meta-product.

This peculiarity may be explained by two successive reactions, oxidation and reduction (see above).

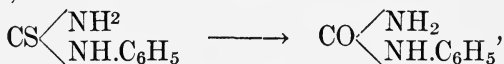
The  $\text{CH}_3$  group is sometimes oxidized by fusion with potash:



Soda may be used instead of potash; but, as its action is not so energetic, it is necessary to prolong the time of fusion at a higher temperature.

#### D. Displacement of Sulphur by Oxygen.

This substitution (exchange of two valences of the carbon atom) is readily effected by the oxides or salts of the heavy metals ( $\text{PbO}$ ,  $\text{HgO}$ ,  $\text{AgNO}_3$ , ammoniacal solution of a silver salt, etc.), and sometimes also by alkalies. Thus, thiophenyl-urea gives phenyl-urea,



by boiling the aqueous or alcoholic solution with  $\text{PbO}$ , or freshly precipitated  $\text{HgO}$ .

With silver nitrate, the reaction is not always complete, intermediate compounds being formed. With allyl-thio-urea,

for instance, there is first formed  $\text{CS} \begin{smallmatrix} \text{NH}_2 \\ \text{NH.C}_3\text{H}_5 \end{smallmatrix} .\text{AgNO}_3$ , which, on moderately heating with  $\text{AgNO}_3$ , is decomposed into  $\text{CO} \begin{smallmatrix} \text{NH}_2 \\ \text{NH.C}_3\text{H}_5 \end{smallmatrix} + \text{Ag}_2\text{S} + 2\text{HNO}_3$ ; this being kept neutral by adding baryta-water from time to time.

The dithionic acids, like  $\text{C}_6\text{H}_5.\text{CS}.\text{SH}$ , lose S on boiling with an alcoholic solution of potash.

Oxidations which take place with the fixation of water will be taken up under Chapter V.

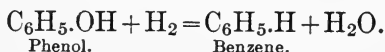
## CHAPTER II.

### REDUCTION.

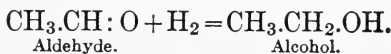
#### I. GENERAL CONSIDERATIONS.

REDUCTION is the opposite of oxidation. It may occur in several different forms:

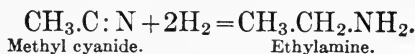
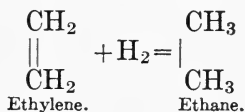
(1) *Reduction of hydroxyl oxygen, as,*



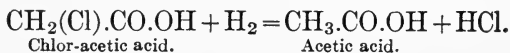
(2) *Reduction of ketonic oxygen to hydroxyl:*



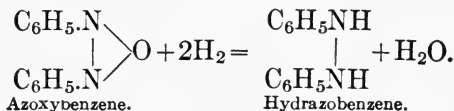
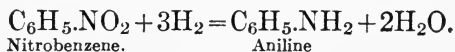
(3) *Reduction of unsaturated groups:*



(4) *Reduction of halogen compounds:*

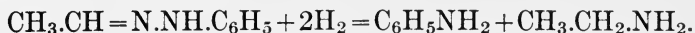


(5) *Reduction of nitro derivatives:*





(6) *Reduction attended by a decomposition of the molecule:* thus, the phenylhydrazine compound of acetaldehyde, when reduced with sodium amalgam, gives rise to two separate amines, aniline and ethylamine:



## II. ACTION OF REDUCING AGENTS.

Though the most logical reagent for reduction purposes would be hydrogen in its nascent condition, yet it does not appear to have met with success as a reducing agent for organic compounds. Attempts have been made, however, to employ electrolytically prepared nascent hydrogen, but the results have not been gratifying. By using this means, Häussermann,<sup>1</sup> in acting on nitrobenzene dissolved in alcoholic caustic soda, obtained hydrazo-benzene and benzdine sulphate; aniline was only produced when a cathode of zinc, instead of platinum, was used.

The majority of reactions involving the reduction of organic compounds take place indirectly through the use of various reducing agents, of which the following are the most important:

**Hydriodic acid** is probably the strongest reducing agent employed in connection with organic compounds. Its action depends on the readiness with which it decomposes into free iodine and hydrogen; it may be employed dissolved either in water or in acetic acid. According to Berthelot, who was the first to recognize its reducing action on organic substances, hydriodic acid is capable of reducing every organic compound to the limit hydrocarbon containing the same number of carbon atoms. He recommended heating the substance to be reduced with a large excess of hydriodic acid in a sealed tube for several hours at a temperature of 275° C. The action of hydriodic acid may be considerably accelerated by the addition of phosphorus,<sup>2</sup>

<sup>1</sup> *Chem. Zeit.*, 1893, p. 129.

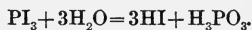
<sup>2</sup> The increased efficiency of the hydriodic acid due to the addition of phosphorus may be accounted for by the fact that the phosphorus combines with the free iodine liberated in the reduction to form phosphorus iodide; and the

which also has the advantage of preventing the formation of undesirable by-products. It is probable that, in the reaction between phosphorus and hydriodic acid, phosphonium iodide is formed as an intermediate step in the reduction. By the use of phosphorus and hydriodic acid, it is possible to carry out a large number of reductions without the necessity of heating in a sealed tube, simply boiling the compound to be reduced with strong hydriodic acid in a flask connected with an inverted condenser and adding fragments of phosphorus from time to time.<sup>1</sup> For some reductions yellow phosphorus is required, while, for others, red phosphorus may be used. In cases where very energetic reduction is necessary, however, recourse must be had to the method of heating the mixture in a sealed tube to a high temperature, and with a large excess of hydriodic acid.<sup>2</sup>

**Sodium** and **sodium amalgam** are largely employed as reducing agents, as they are very efficient and may be applied conveniently. Sodium is mostly used in connection with an alcoholic solution of the substance to be reduced, though, at times, either water or ether may be employed as the solvent. There appears to be a considerable difference in the action of sodium as a reducing agent, depending on the nature of the alcohol employed as the solvent; when amyl alcohol, for instance, is used as the medium, the reducing power of the sodium appears to be greater than with ethyl or methyl alcohols. Sodium amalgam is less energetic in its action than sodium. An

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latter in the presence of water (also generally present as a by-product in the reduction) further reacts to give hydriodic and phosphorous acids. So, in reality, by the intervention of the phosphorus, the iodine is used over and over again to effect the reduction; while at the same time the phosphorus also removes the water, the presence of which would soon limit the reaction, or cause the formation of secondary products:



<sup>1</sup> In this manner iodoform,  $\text{CHI}_3$ , may be reduced to methylene iodide,  $\text{CH}_2\text{I}_2$  (see Baeyer, *Berichte*, vol. v, p. 1095).

<sup>2</sup> By employing this method of reduction, anthracene,  $\text{C}_{14}\text{H}_{10}$ , may be reduced to the hydrocarbon  $\text{C}_{14}\text{H}_{14}$ . (See Lucas, *Berichte*, vol. xxi, p. 2510).

amalgam containing about  $2\frac{1}{2}$  per cent. of sodium is generally employed, as this is solid and may be readily pulverized. Sodium amalgam is most efficient when used in the presence of carbon dioxide, and it may be employed in alcoholic, ethereal, or acetic acid solutions. As sodium hydrate is formed in the course of the reaction with sodium amalgam, the efficiency and speed of the reduction may be increased by neutralizing the alkali with acids.

Metallic tin and stannous chloride are also employed extensively as reducing agents. Tin itself is principally used in connection with hydrochloric acid, and the metal is afterwards removed by precipitation with hydrogen sulphide. Stannous chloride is used in acid solution, and, as it is soluble in alcohol, it may be conveniently employed with this solvent; it may also be used with glacial acetic acid. Sometimes an alkaline solution of tin (sodium stannite) is employed for reductions. This solution is best prepared by adding powdered stannous chloride to a strong solution of sodium hydrate until a precipitate begins to form.

Zinc may be employed for the reduction of organic compounds in either acid or alkaline solutions, and at times even in neutral solution. Zinc dust when used at high temperatures is a powerful reducing agent; even when boiled with water, zinc dust is capable of reducing many substances.

### III. SUBSTITUTION OF HYDROGEN FOR HYDROXYL OR OTHER ELEMENT, GROUP, OR RADICAL.

#### A. Reduction of Hydroxyl and Ketonic Compounds.

(1) **Reduction of Acids.**—In certain cases acids are converted into aldehydes by displacing the OH group with H. Benzoic and oxy-benzoic acids behave in this manner. The first, on treatment with sodium amalgam in the presence of water, gives benzaldehyde; but the second one is converted into the corresponding alcohol. The indirect method which would lead

to the same result consists in heating the salt of the acid with a formate, or in reducing the chlorides or anhydrides of the acids. In the latter case, by an energetic reduction, the corresponding alcohols may be obtained.<sup>1</sup> The reduction of succinyl chloride, however, with sodium amalgam and acetic acid, does not appear to give the corresponding aldehyde, but the lactone of  $\gamma$ -oxybutyric acid. Phthalyl chloride behaves in the same manner. Under the influence of more energetic agents, such as hydriodic acid, acids are converted into hydrocarbons by conversion of the CO.OH group into CH<sub>3</sub>. Thus, stearic acid, C<sub>18</sub>H<sub>36</sub>O<sub>2</sub>, gives a hydrocarbon, C<sub>18</sub>H<sub>38</sub>, and benzoic acid, C<sub>7</sub>H<sub>6</sub>O<sub>2</sub>, gives toluene, C<sub>7</sub>H<sub>8</sub>.

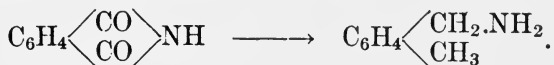
According to Berthelot, reduction by means of hydriodic acid takes place in the following manner: The acid to be reduced is heated on an oil-bath to 200–280° C. with 20 to 30, or even 100 times its weight of hydriodic acid (sp. gr.=1.8 to 2). The tubes are opened from time to time in order to allow of the escape of gas, which may be collected over mercury when it is desired to analyze it. On account of the great pressure which exists in the tubes, they must be opened in a very careful manner. The reduction of the fatty acids, and of products obtained by the action of phosphorus pentachloride on ketones, according to Kraft, takes place in the following manner: In each tube there is placed 2 to 4 grams of the acid, together with 2 to 4 times the quantity of hydriodic acid (sp. gr.=1.7) and  $\frac{1}{3}$  part of red phosphorus; the tubes are heated for 3 to 5 hours at 210–240° C., after which they are opened. A small amount of phosphorus is added, and the tubes are reheated to 210–240° C. These operations are repeated two or three times, and finally water is added to decompose the iodide of phosphorus which is formed. The hydrocarbons are distilled in steam, and then heated with a solution of caustic alkali.

But little is known concerning the reduction of acid amides and imides. Sodium amalgam with acetamide gives a small

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<sup>1</sup> See Zaytzeff, *A New Method for the Conversion of Aliphatic Acids into the Corresponding Alcohols*, Kagan, 1870 (in Russian).

quantity of alcohol. The action of sodium in amyl alcohol on phthalimide reduces the two CO groups:



(2) **Reduction of Aldehydes.**—Aldehydes are converted into alcohols by the action of sodium amalgam in an acidulated ( $\text{H}_2\text{SO}_4$ ) aqueous solution; the alcohol so formed is separated by distillation, the distillate being further treated with potassium carbonate. The higher aldehydes of the aliphatic series, which are difficultly soluble in water, are reduced by the use of zinc dust in glacial acetic acid solution; in this case, however, the reaction results, not in the formation of the alcohol, but of the corresponding acetic ester, which must be saponified in order to obtain the alcohol.

Derivatives of chlor-substituted aldehydes, such as chloral, are reduced to the corresponding alcohols by zinc ethyl; thus, chloral gives tri-chlor-alcohol. In order to reduce aromatic aldehydes it is necessary to suspend them in water or dissolve them in dilute alcohol.<sup>1</sup> For the reduction, an alcoholic solution of potash may be used:



The aromatic aldehydes are also converted into amines by the action of ammonium formate; for example, the conversion of benzaldehyde,  $\text{C}_6\text{H}_5.\text{CHO}$ , into benzylamine,  $\text{C}_6\text{H}_5.\text{CH}_2.\text{NH}_2$ . By the prolonged action at  $130^\circ$ – $150^\circ$  C. of a concentrated solution of hydriodic acid and red phosphorus, aldehydes are converted into hydrocarbons (substitution of **CHO** by **CH<sub>3</sub>**):



(3) **Reduction of Ketones and Quinones.**—The conversion of the **CO** group into **CH.OH** or **C.OH**, and the production of

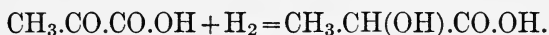
<sup>1</sup> The aromatic aldehydes are liable to form condensation products.

<sup>2</sup> For the action of halogen acids on methylene oxide, see *Jour. Soc. Phys.-Chim. Russe*, vol. 19, p. 169.

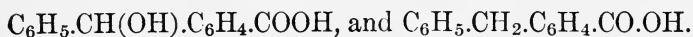
alcohols and phenols by the aid of ketones and quinones, takes place by the action of sodium, or its amalgam in the presence of water, by boiling with a solution of alcoholic potash in the presence of zinc powder, and even by the action of sulphurous acid. Quinone,  $C_6H_4O_2$ , is readily converted into hydroquinone; so much so, in fact, that, in an alcoholic solution under the influence of sunlight, the quinone changes the alcohol into aldehyde.

The ketone, dissolved in ether or benzene, is placed in a flask with water; there is then added small shavings of metallic sodium, which maintain themselves between the two liquids. It is usually necessary to moderate the energy of the reaction by cooling. When the odor of the ketone has disappeared, the upper layer of liquid is removed, and the alcohol produced is isolated by crystallization or distillation. There are also formed condensation products.

The ketonic acids behave like the ketones; thus, pyruvic acid gives lactic acid with sodium amalgam in the presence of water:



In order to avoid the decomposition of certain ketonic acids by the alkali, it is necessary to keep the temperature from rising too high, and to neutralize from time to time with an acid. In certain cases, by the reduction of ketonic acids, there are formed lactones in place of oxyacids; and sometimes the latter, which may be formed at first, are reduced in their turn. For instance, benzophenone-meta-carboxylic acid,  $C_6H_5.CO.C_6H_4.CO.OH$ , with sodium amalgam, is converted into benzo-hydroxy-meta-carboxylic acid:



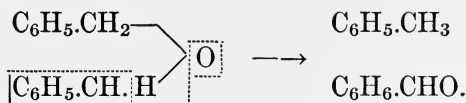
The conversion of the **CO** group into **CH<sub>2</sub>**, and the formation of hydrocarbons with the aid of ketones, is brought about by the action of hydriodic acid under the same conditions as for

aldehydes, or by distillation with zinc dust. Thus, benzophenone,  $(\text{C}_6\text{H}_5)_2\text{CO}$ , gives diphenylmethane,  $(\text{C}_6\text{H}_5)_2\text{CH}_2$ .<sup>1</sup>

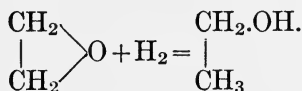
(4) **Reduction of Alcohols.**—The reduction of alcohols (conversion of **OH** into **H**) usually takes place in an indirect manner. The reduction of phenols (such as the conversion of phenol,  $\text{C}_6\text{H}_5\text{OH}$ , or of pyrogallol,  $\text{C}_6\text{H}_3(\text{OH})_3$ , into  $\text{C}_6\text{H}_6$ ) is brought about by distillation with zinc dust or with phosphorus pentasulphide. Oxypyridine and quinoline are also reduced with zinc dust. Cuminic alcohol,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{CH}(\text{CH}_3)_2 \\ \text{CH}_2\text{OH} \end{smallmatrix}$ , on dis-

stillation with zinc dust, gives cymene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{CH}_2\text{CH}_2\text{CH}_3 \\ \text{CH}_3 \end{smallmatrix}$ .

Certain reductions of aromatic alcohols are accompanied by an oxidation: benzyl alcohol, with alcoholic potash, gives toluene and benzoic acid. The simple ethers of aromatic alcohols are separated by heat into aldehydes and hydrocarbons; benzyl ether gives benzaldehyde and toluene:



Hydriodic acid and red phosphorus, on heating, furnish a good means of reduction for alcohols of the paraffin series, as well as those of the aromatic series having the OH in a side chain, and also oxyacids. Aromatic lactones or phthaleins are also reduced with zinc powder in alkaline solution, and yield phthalines. Ethylene oxide is readily converted into alcohol with sodium amalgam:



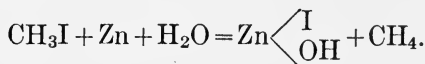
This reaction may be considered as a reduction followed by a fixation of water. The reverse reaction—reduction with

<sup>1</sup> The keto-phenone,  $\text{C}_6\text{H}_5\text{CO}\cdot\text{CH}_3$ , treated with hydriodic acid, does not give ethyl-benzene,  $\text{C}_6\text{H}_5\text{C}_2\text{H}_5$ , but condensation products.





and regular current may be obtained containing only a small quantity of the vapors of alcohol and methyl iodide. Two c.c. of  $\text{CH}_3\text{I}$  give 700 c.c. of  $\text{CH}_4$ . The reaction may be expressed as follows:



In order to replace halogens in an aromatic nucleus, it is necessary to use sodium amalgam in the presence of water, or hydriodic acid with phosphorus in sealed tubes. Metals with acids react but seldom and very slowly; while, on the contrary, the halogens in side-chains are displaced very easily. Chlorine in the pyridine nucleus is removed by tin and hydrochloric acid:



Also, in the chlorides of organic acids, the halogen is easily replaced. The chlorides of the sulphonic acids behave in a similar manner: thus,  $\text{R}.\text{SO}_2\text{Cl}$  is converted into  $\text{R}.\text{SO}_2\text{H}$ . The reduction should take place in an alkaline solution; in acid solution the reduction goes still further, and a mercaptan is formed,  $\text{R}.\text{SH}$ . Sometimes the reduction is accompanied by a decomposition of the molecule; chlor-sulphocymene,  $\text{C}_{10}\text{H}_7.\text{SO}_2.\text{Cl}$ , with sodium amalgam, gives  $\text{C}_{10}\text{H}_8$  and  $\text{SO}_2$ .

It is easy to remove bromine when combined with oxygen in derivatives, as in phenol bromide,  $\text{C}_6\text{H}_5.\text{OBr}$ . Tribrom-phenol-bromide,  $\text{C}_6\text{H}_2 \begin{array}{c} \text{Br}_3 \\ \diagup \\ \text{OBr} \end{array}$ , loses bromine on boiling with alcohol, giving tribrom-phenol,  $\text{C}_6\text{H}_2 \begin{array}{c} \text{Br}_3 \\ \diagup \\ \text{OH} \end{array}$ .

Several halogen atoms may be replaced successively in the combinations in which they occur. In compounds of the paraffin series, if the halogens occur with neighboring carbon atoms, instead of a simple replacement of the halogen, there is generally a rupture of the molecule, with the formation of unsaturated compounds. On partial reduction with hydriodic

acid, for instance, propylene chloride,  $\text{CH}_3.\text{CH}(\text{Cl}).\text{CH}_2\text{Cl}$ , gives isopropyl chloride,  $\text{CH}_3.\text{CHCl}.\text{CH}_3$ , and propylene bromide,  $\text{CH}_3.\text{CH}(\text{Br}).\text{CH}_2\text{Br}$ , gives isopropyl bromide,  $\text{CH}_3.\text{CHBr}.\text{CH}_3$ . The compound,  $\text{CH}_3.\text{CH}(\text{Cl}).\text{CH}_2\text{I}$ , treated with the theoretical quantity of hydriodic acid, is converted into isopropyl chloride,  $\text{CH}_3.\text{CH}(\text{Cl}).\text{CH}_3$ ; with an excess, there is formed isopropyl iodide,  $\text{CH}_3.\text{CH}(\text{I}).\text{CH}_3$ .

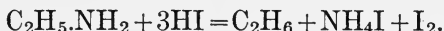
(2) **Substitution of the Nitrile Radical (CN).**—(See page 62.)

(3) **Substitution of the Nitro Group ( $\text{NO}_2$ ).**—(See page 65.)

By the use of diazo compounds, see the substitution of  $-\text{N}:\text{NR}$  by  $\text{H}$ .

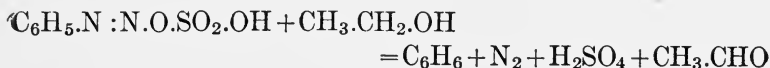
(4) **Substitution of the Nitroso Group (NO).**—This is brought about by boiling nitroso-compounds with concentrated hydrochloric acids. Thus, nitroso-dimethylaniline,  $(\text{CH}_3)_2\text{N}.\text{NO}$ , is converted into a salt of dimethylaniline. The same result is obtained by using a solution of alcoholic potash, or certain other reducing agents (see page 63).

(5) **Substitution of the Amido Group ( $\text{NH}_2$ ).**—This reaction is rarely produced directly. Ethylamine at  $275^\circ\text{C}$ ., with hydriodic acid, is decomposed according to the equation:



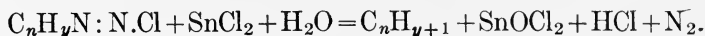
For the use of the azo derivatives in effecting this reaction, see the substitution of  $\text{N}:\text{NR}$  by  $\text{H}$ .

(6) **Substitution of the Diazo Group ( $-\text{N}:\text{NR}$ ).**—This reaction often takes place. Into an acid solution of the sulphate or nitrate of an amine a slow current of  $\text{N}_2\text{O}_3$  is passed (it is best to use theoretical quantities). The salt of the diazo derivative which is formed (diazo-benzene-sulphate,  $\text{C}_6\text{H}_5.\text{N}:\text{N}.\text{O}.\text{SO}_2.\text{OH}$ , for example) is isolated by alcohol and ether, and then decomposed by boiling with absolute alcohol, according to the equation:

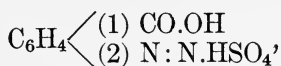


The separation of the diazo-salt may be dispensed with; the amido compound is dissolved in a mixture of concentrated sulphuric acid and alcohol; there is then added the theoretical quantity of a concentrated aqueous solution of sodium nitrite or an excess of ethyl or amyl nitrite.

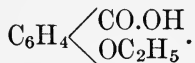
The diazo-chlorides are decomposed in the same manner by means of stannous chloride. If an excess of stannous chloride is added to a cold dilute solution of the diazo-chloride (1 mol.  $\text{NaNO}_2$ , 1 mol. amine, 2 mols.  $\text{HCl}$ ), the following reaction will take place:



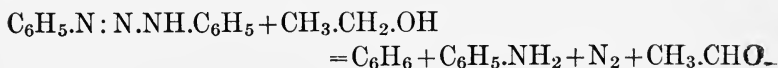
In this reaction there are probably formed some hydrazines as secondary compounds. Hydrazines may also be used to replace  $\text{N:N.R}$  by  $\text{H}$ , for, by boiling them with copper sulphate, they are decomposed with evolution of  $\text{N}_2$ . Thus, phenylhydrazine,  $\text{C}_6\text{H}_5.\text{NH.NH}_2$ , gives benzene,  $\text{C}_6\text{H}_6$ . In certain cases, boiling the diazo body with alcohol causes the  $\text{N:N.R}$  to be replaced, instead of by  $\text{H}$ , by  $\text{O.C}_2\text{H}_5$ . For instance, while the ortho-diazo-benzoic acid sulphate,



gives only benzoic acid by this reaction, the para and meta isomers yield, besides benzoic acid, meta- and para-ethoxybenzoic acids:

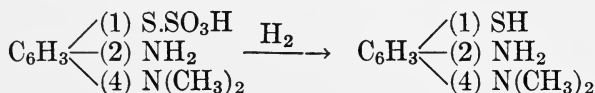


In place of the diazo-salts, the diazo-amido compounds (action of  $\text{N}_2\text{O}_3$  on an alcoholic solution of an amido derivative) may be decomposed by alcohol. Thus:



In this reaction half of the amido compound is reformed, but this may be avoided by treating the substance with a mixture of alcohol and nitrous ether. The diazo-amido compound obtained is decomposed with alcohol, and the amido body which is reformed reacts again with the nitrous ether.

(7) **Substitution of the Sulphonic Acid Group (SO<sub>3</sub>H).**—This is observed in the case of ortho-amido-thiosulphonic acid of dimethylaniline:



By the reduction of this body, a mercaptan is formed.

(8) **Substitution of Oxygen.**—This has already been studied in the reduction of aldehydes, ketones, nitroso derivatives, and oxyazo bodies. The reduction of the latter is identical with that of the azo derivatives.

(9) **Substitution of Sulphur.**—This takes place by the action of zinc (or of zinc dust) and hydrochloric acid, or with sodium amalgam.  $\text{C}_6\text{H}_5.\text{CS}.\text{NH}_2$  is converted into  $\text{C}_6\text{H}_5.\text{CH}_2.\text{NH}_2$ .

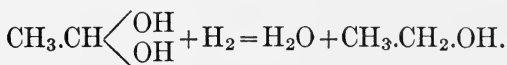
(10) **The Removal of Oxygen.**—This takes place very rarely; in general it is the replacing of OH by H. As an example of the removal of oxygen may be cited the conversion of the sulphinic acids,  $\text{R}.\text{SO}_2\text{H}$ , into mercaptans,  $\text{R}.\text{SH}$ , by zinc dust and dilute sulphuric acid, or with tin and hydrochloric acid. The conver-

sion of azoxy-benzene,  $\text{C}_6\text{H}_5.\text{N} \begin{array}{c} \diagup \\ | \\ \diagdown \end{array} \text{O} \begin{array}{c} \diagdown \\ | \\ \diagup \end{array} \text{N}.\text{C}_6\text{H}_5$ , into azo-benzene,  $\text{C}_6\text{H}_5.\text{N} \parallel \text{N}.\text{C}_6\text{H}_5$ , is not complete.

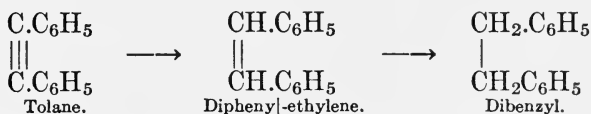
#### IV. FIXATION OF HYDROGEN.

There is a fixation of hydrogen during the reduction of unsaturated compounds, or, in general, in those bodies which have several elements united by more than one bond. We

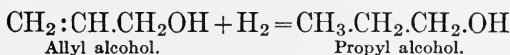
have considered the reduction of aldehydes, not as one of addition of H, but as the replacement of OH by H in the dihydrates:



Hydrocarbons, like ethylene and acetylene, give ethane when heated to 500° C. with hydrogen; at the ordinary temperature, they combine with hydrogen in the presence of platinum black. At 150° C. in sealed tubes, the phenyl derivatives of the unsaturated hydrocarbons fix hydrogen by means of concentrated hydriodic acid. Thus:



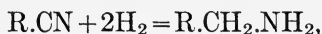
Hydriodic acid permits of the addition of hydrogen to benzene and its numerous derivatives, and there may thus be obtained, by a prolonged reduction, the derivatives of benzene hexahydride. It is more convenient to employ absolute ethyl or amyl alcohol and sodium. In this way may be prepared piperidine,  $\text{C}_5\text{H}_{11}\text{N} = \text{C}_5\text{H}_5\text{N.H}_6$ , from pyridine. Hydrogen cannot be added to the unsaturated alcohols with hydriodic acid, because the iodides are formed; in this case the reducing agent should be sodium amalgam, or zinc with an acid:



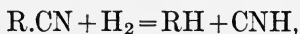
Iron and acetic acid appear to be the best for converting unsaturated aldehydes into the saturated. Under these conditions, the CHO group is often changed into  $\text{CH}_2\text{OH}$ , and sometimes more readily than  $\text{C}=\text{C}$  into  $\text{CH}-\text{OH}$ . Sodium amalgam in alkaline solution is the best for converting the unsaturated acids, like cinnamic acid,  $\text{C}_6\text{H}_5\text{CH}:\text{CH.COOH}$ , into saturated acids, like  $\text{C}_6\text{H}_5.\text{CH}_2.\text{CH}_2.\text{COOH}$ . Those which resist this action, like crotonic acid,  $\text{CH}_3.\text{CH}:\text{CH.COOH}$ , are reduced with hydriodic acid and red phosphorus at 160° C. At 130° C. there

is a fixation of hydriodic acid; the iodo-derivative then reacts with hydriodic acid again with the splitting off of 2 atoms of iodine.

Reduction causes nitriles to pass into amines:

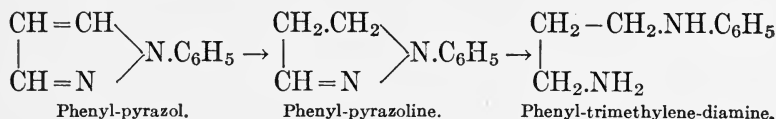


with partial hydrolysis however; besides primary amines, there are also formed secondary and tertiary amines.<sup>1</sup> This reduction is generally effected with zinc and dilute sulphuric or hydrochloric acid in aqueous, alcoholic, or ethereal solution. Sodium in absolute alcohol may also be used. In this case the aromatic nitriles give secondary products, as the reduction takes place partly according to the equation:



with the formation of a hydrocarbon and hydrocyanic acid, and as the amines and hydrocarbons formed also submit to a further fixation of hydrogen.

The pyrazols, with sodium in absolute alcohol, give pyrazolines and diamines:



The oximes are reduced in the same manner to amines, and the group  $>C=N.OH$  becomes  $>CH.NH_2$ . In this manner it is possible to realise the synthesis of aspartic acid by the reduction of the oxime obtained by the action of hydroxylamine on oxalo-acetic ester.<sup>2</sup>

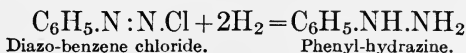
The azo compounds,<sup>3</sup>  $C_6H_5.N=N.C_6H_5$ , are readily con-

<sup>1</sup> See *Gaz. chim. Ital.*, vol. 9, p. 555.

<sup>2</sup> *Ibid.*, vol. 17, p. 519.

<sup>3</sup> Acid reducing agents, like stannous chloride in the presence of sulphuric acid, convert the azo bodies into diamines.

verted into hydrazo bodies,  $\text{C}_6\text{H}_5\text{.NH-NH.C}_6\text{H}_5$ , by sodium amalgam in alcoholic solution, zinc powder, or ammonium sulphide. To use the latter, the compound is dissolved in alcohol, saturated with ammonia, then treated with a current of hydrogen sulphide. The sulphur is separated by filtration; and on the addition of water, the hydrazo body is precipitated. The azo bodies may also be reduced with ferrous sulphate in alkaline solution. It is sufficient to add the ferrous sulphate to an alkaline solution of the compound until the precipitation of ferric hydrate ceases. Acid reducing agents, such as stannous chloride in the presence of sulphuric acid, convert azo bodies into diamines. The diazo compounds are converted into hydrazines by reducing agents like  $\text{SnCl}_2$  in  $\text{HCl}$ :



The hydrazines are decomposed by the fixation of hydrogen.<sup>1</sup>

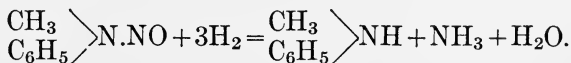
## V. REDUCTION OF NITRO AND NITRO COMPOUNDS.

Nitroso derivatives are converted into amines when the oxygen of the  $\text{NO}$  group is replaced by  $\text{H}_2$ . This reduction is generally brought about by zinc and acetic acid, or with tin and hydrochloric acid.

The reduction of nitrosamines furnishes a method for the preparation of secondary hydrazines:



In certain cases the reaction may proceed in another manner; thus, with the preceding body, it may be:



<sup>1</sup> The hydrazines are bodies derived theoretically from diamidogene,  $\text{H}_2\text{N-NH}_2$ , by substitution of paraffin or aromatic radicals (or alcoholic, phenolic, or acidio radicals), for one or several atoms of hydrogen. There are primary, secondary, tertiary, and quaternary hydrazines.

The reduction of nitroso-anilides proceeds exclusively in this manner, with the evolution of ammonia and the formation of anilides:



When isonitroso bodies are reduced, there is a complication of the molecule. For the reduction of oximes, see p. 62.

It is well known that reduction converts  $\text{NO}_2$  into  $\text{NH}_2$ ; the process of Zinin for obtaining aromatic-amido compounds depends on this reaction. In the paraffin series the reduction of  $\text{NO}_2$  (nitro-ethane, for example) to  $\text{NH}_2$  is probably not at all analogous to that which takes place in the aromatic series.<sup>1</sup> The agents mostly employed for the reduction of nitro compounds are tin and hydrochloric acid, and a solution of stannous chloride in hydrochloric acid. The advantage of these bodies is the ease of separating the tin by sulphuretted hydrogen; in the solution there remains only the chloride of the amido compounds. The amines with a basic character are precipitated from their acid solutions with ammonia; amido-phenols, by sodium carbonate; amido-carboxylic acids, by sodium acetate. The reduction sometimes proceeds in an abnormal manner; thus ortho-nitro-toluene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{---} (1) \text{CH}_3 \\ \text{---} (2) \text{NO}_2 \end{smallmatrix}$ , with tin and hydro-

chloric acid, gives para-chlor-ortho-toluidine,  $\text{C}_6\text{H}_3 \begin{smallmatrix} \text{---} (1) \text{CH}_3 \\ \text{---} (2) \text{NH}_2 \\ \text{---} (4) \text{Cl} \end{smallmatrix}$

$\alpha$ -brom- $\beta$ -nitro-naphthalene,  $\text{C}_{10}\text{H}_6 \begin{smallmatrix} \text{---} \text{Br} \\ \text{---} \text{NO}_2 \end{smallmatrix}$ , with the same reducing agent gives  $\beta$ -naphthylamine,  $\text{C}_{10}\text{H}_7 \cdot \text{NH}_2$ . In such cases, the tin is replaced by iron or zinc dust and acetic acid;

there will then be obtained brom-naphthylamine,  $\text{C}_{10}\text{H}_6 \begin{smallmatrix} \text{---} \text{Br} \\ \text{---} \text{NH}_2 \end{smallmatrix}$ ,

the normal derivative of brom-nitronaphthalene,  $\text{C}_{10}\text{H}_6 \begin{smallmatrix} \text{---} \text{Br} \\ \text{---} \text{NO}_2 \end{smallmatrix}$ .

<sup>1</sup> *Bull. Soc. Chim.*, vol. 46, p. 266.



By a very energetic reduction  $\text{NO}_2$  may be replaced by  $\text{H}$ ; thus, by using a large excess of iron and acetic acid, nitrobenzene,  $\text{C}_6\text{H}_5\cdot\text{NO}_2$ , gives benzene,  $\text{C}_6\text{H}_6$ , and ammonia; and trinitro-mesitylene,  $\text{C}_6\text{H}_2\begin{smallmatrix} \diagup (\text{CH}_3)_3 \\ \diagdown (\text{NO}_2)_3 \end{smallmatrix}$ , gives a cumidine,  $\text{C}_6\text{H}_3\begin{smallmatrix} \diagup (\text{CH}_3)_3 \\ \diagdown (\text{NH}_2)_2 \end{smallmatrix}$ .

When the compound contains several  $\text{NO}_2$  groups, it is easily possible to reduce one after another by means of sulphuretted hydrogen, and in the order that is desired. For example:

dinitro-toluene,  $\text{C}_6\text{H}_3\begin{smallmatrix} \diagup (1) \text{CH}_3 \\ \diagdown (2) \text{NO}_2 \\ \diagdown (4) \text{NO}_2 \end{smallmatrix}$ , with sulphuretted hydrogen

in alkaline solution, cold, gives only ortho-nitro-para-toluidine,

$\text{C}_6\text{H}_3\begin{smallmatrix} \diagup (1) \text{CH}_3 \\ \diagdown (2) \text{NO}_2 \\ \diagdown (4) \text{NH}_2 \end{smallmatrix}$ ; if heat is employed, its isomer is obtained,

$\text{C}_6\text{H}_3\begin{smallmatrix} \diagup (1) \text{CH}_3 \\ \diagdown (2) \text{NH}_2 \\ \diagdown (4) \text{NO}_2 \end{smallmatrix}$ ; if tin and hydrochloric acid in alcoholic solu-

tion are used, the latter body only is obtained.

Sometimes in reductions there occurs an evolution of  $\text{CO}_2$ .

Thus, dinitrobenzoic acid,  $\text{C}_6\text{H}_3\begin{smallmatrix} \diagup (1) \text{COOH} \\ \diagdown (2) \text{NO}_2 \\ \diagdown (4) \text{NO}_2 \end{smallmatrix}$ , gives meta-

phenylene-diamine,  $\text{C}_6\text{H}_4\begin{smallmatrix} \diagup (2) \text{NH}_2 \\ \diagdown (4) \text{NH}_2 \end{smallmatrix}$ . Brom-nitrobenzoic acid,

$\text{C}_6\text{H}_3\begin{smallmatrix} \diagup (1) \text{COOH} \\ \diagdown (2) \text{Br} \\ \diagdown (4) \text{NO}_2 \end{smallmatrix}$ , gives meta-brom-aniline,  $\text{C}_6\text{H}_4\begin{smallmatrix} \diagup (2) \text{Br} \\ \diagdown (4) \text{NH}_2 \end{smallmatrix}$ .

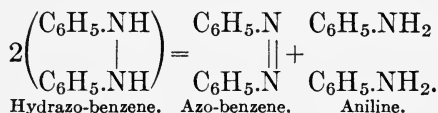
Hence it is necessary to take particular precautions in the reduction of nitro-carboxyl acids. The favorite method is to dissolve them in aqueous ammonia or in baryta-water, and to add ferrous sulphate in a very concentrated solution.

The reduction of nitro-nitriles is surrounded with difficulties. Sulphuretted hydrogen cannot be employed, as it is liable to form a compound with the nitrile; other reducing agents cause a saponification. The best method, in certain cases, is to treat the derivative with tin and glacial acetic acid saturated with hydrochloric acid.

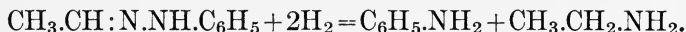
Nitro derivatives are sometimes reduced in a complicated manner.

## VI. REDUCTION WITH DECOMPOSITION OF THE MOLECULE.

This reaction is to be observed in the energetic reduction of hydrazo compounds with tin and hydrochloric acid in a sealed tube. Hydrazo derivatives are reduced similarly when they are heated:



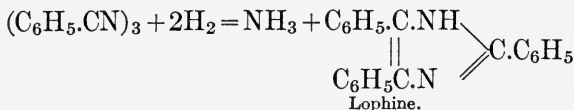
The products of the condensation of aldehydes with hydrazines are decomposed in the same manner. Ordinary aldehyde combined with phenyl-hydrazine gives a compound which, with sodium amalgam, is decomposed into aniline and ethylamine:



Hydrazines alone are decomposed in a similar manner. By prolonged boiling on a water bath with zinc dust and hydrochloric acid, phenyl-hydrazine is decomposed into ammonia and aniline:



Reduction with evolution of ammonia also takes place by the action of ammonia on cyan-phenine,



and by the reduction, with fixation of water (by sodium amalgam), of the cinchomeric acids (pyridine carboxylic acid):



## CHAPTER III.

### SUBSTITUTIONS.

#### I. LAWS OF SUBSTITUTIONS.

By the action of chlorine on hydrocarbons of a normal chain, there are usually obtained two substitution products:

$R.CH_2.CH_2.Cl$  and  $R.CH\begin{smallmatrix} \diagup Cl \\ \diagdown CH_3 \end{smallmatrix}$ , while with bromine there

is almost exclusively obtained  $R.CH\begin{smallmatrix} \diagup Br \\ \diagdown CH_3 \end{smallmatrix}$ . Ethyl benzene

behaves in the same manner on chlorination or bromination in sunlight; there is formed exclusively chlor-ethyl-benzene,

$C_6H_5.CH\begin{smallmatrix} \diagup Cl \\ \diagdown CH_3 \end{smallmatrix}$ , or the corresponding bromine derivative.

Secondary hydrocarbons are substituted by chlorine at the carbon atom containing the least number of hydrogen atoms:



On further action the chlorine attaches to the carbon atom which adjoins that one already linked to a halogen. In certain cases, however, this rule does not hold.

1st. With ethylidene chloride,  $CH_3.CH.Cl_2$ , besides tri-chlor-ethane,  $CH_3.CCl_3$ , there is produced at the same time chlor-ethylene chloride,  $CH_2Cl.CHCl_2$ .

2d. During the chlorination in sunlight of iso-propyl chloride,  $CH_3.CHCl.CH_3$ , there is formed, simultaneously with iso-propylidene chloride,  $CH_3.CCl_2.CH_3$ , a certain quantity of propylene chloride,  $CH_3.CHCl.CH_2Cl$ . The latter is formed exclusively with iodine chloride,  $ICl$  (at  $100^\circ C.$ ); by the continued action of iodine chloride, this is finally converted

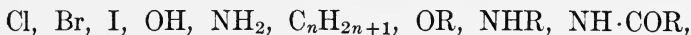
into trichlorhydrin of glycerol,  $\text{CH}_2\text{Cl}.\text{CHCl}.\text{CH}_2.\text{Cl}$ . This reaction is interesting, as it allows of the synthesis of glycerol.

3d. Ethyl bromide,  $\text{C}_2\text{H}_5.\text{Br}$ , at  $200^\circ\text{C}$ ., with bromine gives ethylidene bromide,  $\text{CH}_3.\text{CHBr}_2$ ; but in the presence of aluminium bromide,  $\text{Al}_2\text{Br}_6$ , there is formed only the bromide of ethylene,  $\text{CH}_2\text{Br}.\text{CH}_2\text{Br}$ . Propyl and iso-propyl bromides,  $\text{CH}_3.\text{CH}_2.\text{CH}_2\text{Br}$ , and  $\text{CH}_3.\text{CHBr}.\text{CH}_3$ , on bromination, both yield the same propylene bromide,  $\text{CH}_3.\text{CHBr}.\text{CH}_2\text{Br}$ .

Fatty acids with halogens yield principally the  $\alpha$ -derivatives. Propionic acid with bromine gives the  $\alpha$ -brom and  $\alpha$ -di-brom-propionic acids:



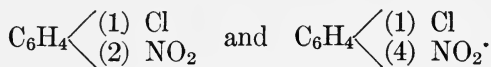
The aromatic series affords the most general laws.<sup>1</sup> It may be said that usually the introduction into a compound of substituents of the first group,



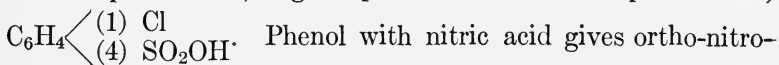
will usually cause the second substituting group to go to the ortho and para positions, while substituents of the second group,



will usually form meta compounds with the second radical. Thus, chlor-benzene,  $\text{C}_6\text{H}_5\text{Cl}$ , with nitric acid, gives a mixture of ortho- and para-chlor-nitrobenzenes:



With sulphuric acid, it gives para-chlor-benzene sulphonic acid,



Phenol with nitric acid gives ortho-nitro-phenol,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{OH} \\ \text{NO}_2 \end{smallmatrix} \begin{smallmatrix} (1) \\ (2) \end{smallmatrix}$ , and para-nitro-phenol,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{OH} \\ \text{NO}_2 \end{smallmatrix} \begin{smallmatrix} (1) \\ (4) \end{smallmatrix}$ .

Nitro-benzene with nitric acid yields principally meta-dinitro-

<sup>1</sup> See Armstrong, *Jour. Chem. Soc.*, 1887.

benzene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{NO}_2 \\ \searrow (3) \text{NO}_2 \end{smallmatrix}$ , with but a small amount of the ortho and para isomers. Occasionally two different groups have the same action on the substituant. Thus, para-nitrotoluene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{CH}_3 \\ \searrow (4) \text{NO}_2 \end{smallmatrix}$ , on chlorination gives  $\text{C}_6\text{H}_3 \begin{smallmatrix} \swarrow (1) \text{CH}_3 \\ \searrow (2) \text{Cl} \\ \searrow (4) \text{NO}_2 \end{smallmatrix}$ ; and meta-nitro-benzoic acid,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{COOH} \\ \searrow (3) \text{NO}_2 \end{smallmatrix}$ , on nitration

yields  $\text{C}_6\text{H}_3 \begin{smallmatrix} \swarrow (1) \text{CO}_2\text{OH} \\ \searrow (3) \text{NO}_2 \\ \searrow (5) \text{NO}_2 \end{smallmatrix}$ . Sometimes, however, the action is

different, and then isomers are formed. Thus, if brom-nitrotoluene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{CH}_3 \\ \searrow (4) \text{Br} \end{smallmatrix}$ , is treated with sulphuric acid, the  $\text{CH}_3$  group has the tendency to make the sulphonic acid group take the positions 2 or 6, while that of the bromine would make it take positions 3 or 5, and, as a result, two isomers are formed. It may happen that the influence of one group is stronger than that of another, as in the case of para-brom-aniline, where  $\text{NH}_2$  has more influence than  $\text{Br}$ , and hence

on nitration there is formed  $\text{C}_6\text{H}_3 \begin{smallmatrix} \swarrow (1) \text{NH}_2 \\ \searrow (2) \text{NO}_2 \\ \searrow (4) \text{Br} \end{smallmatrix}$ . In the same way  $\text{OH}$  and  $\text{NH.CO.CH}_3$  have more influence than  $\text{CH}_3$ .

External conditions also have an influence on the formation of isomers. Thus, phenol in the cold, with sulphuric acid, gives principally aseptol,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{OH} \\ \searrow (2) \text{SO}_2\text{OH} \end{smallmatrix}$ , and with nitric acid it gives  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{OH} \\ \searrow (4) \text{NO}_2 \end{smallmatrix}$ ; if heat is employed, however, in the first case, para-phenol-sulphonic acid,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{OH} \\ \searrow (4) \text{SO}_2\text{OH} \end{smallmatrix}$ , will be formed, and, in the second case, ortho-nitro-phenol,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow (1) \text{OH} \\ \searrow (2) \text{NO}_2 \end{smallmatrix}$ .

The action of halogens on the aromatic hydrocarbons will differ according to the temperature and the conditions

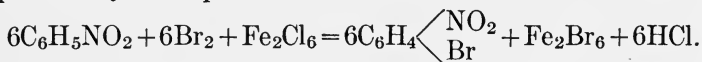
of light, and there will correspondingly be produced substitutions in the nucleus or in the side-chains. If chlorine is allowed to act on boiling toluene, or on its vapors, or even when cooled to zero but in direct sunlight, the side-chain will suffer substitution; the principal product, for example, being benzyl chloride,  $C_6H_5.CH_2.Cl$ . At the ordinary temperature, or even with heat, but in the presence of a chlorine carrier, the substitution takes place in the nucleus, and chlor-toluene,  $C_6H_4\begin{smallmatrix} \diagup CH_3 \\ \diagdown Cl \end{smallmatrix}$ , is formed. Bromine acts in the same manner.

In certain cases, external conditions only influence the rapidity of the reaction, but not its direction. Thus, dry chlorine on acetophenone,  $C_6H_5.CO.CH_3$ , whether cold or hot, in sunlight or in the dark, gives principally the compound  $C_6H_5.CO.CH.Cl_2$ .

## II. SUBSTITUTION OF CERTAIN ELEMENTS OR GROUPS BY OTHERS.

### A. Preparation of Halogen Compounds.

The exchange of hydrogen for a halogen frequently takes place by direct action at  $15^\circ C.$ , or by heating (as when the vapors of a body, mixed with chlorine or bromine, are allowed to pass through animal charcoal heated to  $250-400^\circ C.$ ). The presence of certain bodies greatly facilitates the formation of substituted halogen compounds. Iodine, or the chlorine and bromine compounds of molybdenum, iron, aluminium, and antimony, aid considerably in bromination or chlorination. Ferric chloride is also an agent for bromination or iodination, but it does not remain unaltered as in chlorination, or as is the case with most agents serving as halogen-carriers. Sulphuric acid also acts as a carrier of iodine. The bromination of nitro-benzene in the presence of ferric chloride may be expressed by the equation:



An analogous reaction occurs in that of iodine on benzene

in the presence of ferric chloride, but the quantity of iodo-benzene produced is very small. The ferric chloride should be absolutely dry, else the reaction will take place in another direction. Thus, when para-nitro-toluene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{(1) CH}_3 \\ \text{(4) NO}_2 \end{smallmatrix}$ , is heated with bromine and moist ferric chloride, it is converted into para-nitro-benzyl-chloride,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{(1) CH}_2\text{Cl} \\ \text{(4) NO}_2 \end{smallmatrix}$ .

In certain cases, to chlorinate a body it is heated in a sealed tube with iodine trichloride, antimony pentachloride, phosphorus pentachloride, or calcium hypochlorite. There may also be employed, as a source of chlorine, a mixture of hydrochloric acid and manganese dioxide, or potassium bichromate with potassium chlorate.

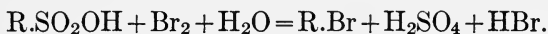
On heating xylene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{(1) CH}_3 \\ \text{(4) CH}_3 \end{smallmatrix}$ , with phosphorus pentachloride at 190–195° C., according to the quantity chlorinated, there is formed  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{(1) CH}_2\cdot\text{Cl} \\ \text{(4) CH}_2\cdot\text{Cl} \end{smallmatrix}$  or even  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{(1) CHCl}_2 \\ \text{(4) CHCl}_2 \end{smallmatrix}$ .

Iodine trichloride though acting as a chlorine carrier, in certain cases also gives iodine substitution products. For example,  $\text{CO} \begin{smallmatrix} \text{CH}_3 \\ \text{CH}_3 \end{smallmatrix}$  with  $\text{ICl}_3$  gives  $\text{CO} \begin{smallmatrix} \text{CH}_2\text{I} \\ \text{CH}_2\text{I} \end{smallmatrix}$ .

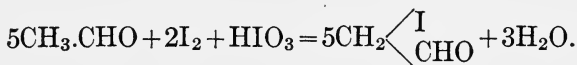
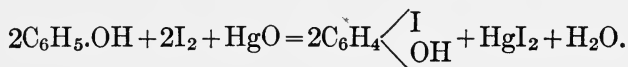
The addition of water favors bromination. The presence of red phosphorus allows of the preparation of bromine compounds without heating in a sealed tube. The hydrobromic acid which is liberated during bromination may cause secondary reactions,—for example, reduction of the  $\text{NO}_2$  group. Thus, by the action of bromine on nitro-benzene in the presence of bromine carriers, there is formed brom-nitro-benzene,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{Br} \\ \text{NO}_2 \end{smallmatrix}$ , and simultaneously there is also formed tribrom-aniline,  $\text{C}_6\text{H}_2 \begin{smallmatrix} \text{Br}_3 \\ \text{NH}_2 \end{smallmatrix}$ , and tetrabrom-aniline,  $\text{C}_6\text{H} \begin{smallmatrix} \text{Br}_4 \\ \text{NH}_2 \end{smallmatrix}$ .

Nitro compounds, when brominated or chlorinated, often exchange their  $\text{NO}_2$  group for a Br or Cl. Thus, with the nitro-benzoic acids, there is formed brom-benzoic acid and

brom-benzene (resulting from the elimination of  $\text{CO}_2$ ). The sulphonic acids behave somewhat in the same manner; with bromine they give brominated compounds and at the same time exchange  $\text{SO}_2\text{OH}$  for  $\text{Br}$ :



The formation of halogen acids, during the action of halogens, has a bad influence on the reaction, especially when under the influence of iodine. It is necessary in this case to eliminate the hydriodic acid which is formed; this may be done by adding with the iodine some mercury oxide,  $\text{HgO}$ , or iodic acid,  $\text{HIO}_3$ . The reaction may then be expressed as follows:

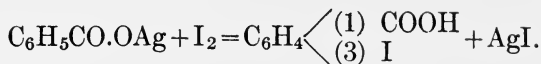


Phenols and the aromatic oxy-acids react readily with iodine and iodic acid. With hydrocarbons and carboxylic acids, it is necessary to heat them with the same reagents in sealed tubes to  $200\text{--}240^\circ \text{C}$ . Iodine and mercuric oxide may also be made to react in alcoholic solution or in glacial acetic acid. Solvents serving for chlorination are chloroform and carbon disulphide, never alcohol or ether; for bromination, besides the preceding, there may also be used glacial acetic acid or petroleum ether. Salicylic acid is converted into iodo-salicylic acid when heated with an alcoholic solution of iodine. It is probable that the hydriodic acid formed is decomposed by the alcohol; for otherwise it would reduce, even below  $100^\circ \text{C}$ ., the iodo-salicylic acid to salicylic acid again.

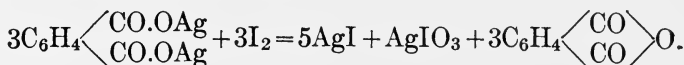
Iodination is readily performed by means of iodine chloride,  $\text{ICl}$ . Thus,  $\text{C}_6\text{H}_5.\text{CH}_3 + \text{ICl} = \text{HCl} + \text{C}_6\text{H}_4\begin{matrix} \text{CH}_3 \\ \diagup \\ \text{I} \end{matrix}$ . Some acids may be brominated or iodinated by the action of bromine or



iodine on their silver salts:



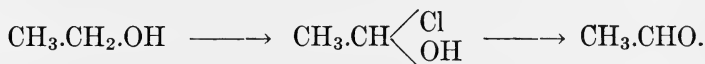
Certain acids, however, behave differently. The salt of phthalic acid is decomposed with the formation of the anhydride:



The halogen sometimes reacts so energetically that it is difficult to obtain monohalogen substituted products,—for example, the chlorination of aromatic amines (see page 74 for the aliphatic amines). Aniline,  $\text{C}_6\text{H}_5\cdot\text{NH}_2$ , with chlorine, immediately gives trichlor-aniline,  $\text{C}_6\text{H}_2 \begin{array}{c} \text{Cl}_3 \\ \text{NH}_2 \end{array}$ . To prepare

chlor-aniline,  $\text{C}_6\text{H}_4 \begin{array}{c} \text{Cl} \\ \text{NH}_2 \end{array}$ , it is necessary to first transform the aniline into an anilide, then chlorinate, and finally saponify.

The alcohols of the paraffin series, by reason of the oxidation which accompanies chlorination, give chlor-aldehydes. By the action of chlorine on ethyl alcohol, it may be supposed that there is formed a chlor-ethyl alcohol, which is decomposed into aldehyde and hydrochloric acid:

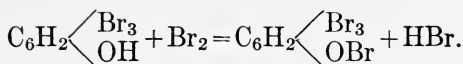


The chlorine substitution products of the alcohols are only formed from polyatomic alcohols or chlor-aldehydes.

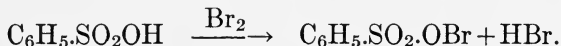
In certain rare cases, the hydrogen not linked to carbon may be replaced by a halogen. Phenol, or its tribrom- or trichlor-derivatives, with an excess of bromine water, has its phenolic hydrogen replaced by bromine:<sup>1</sup>

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<sup>1</sup> This characteristic reaction of the phenol is based on the formation of the tribrom-phenol bromide, and not on the formation of tribrom-phenol. The tribrom-phenol bromide,  $\text{C}_6\text{H}_2\text{Br}_3\cdot\text{OBr}$ , is not attacked by boiling alkalies; its solu-



The aromatic sulphonic acids, with bromine, yield compounds in which the acid hydrogen is replaced by bromine:



In acid amides, the halogen replaces the hydrogen attached to the nitrogen, by action in alkaline solution. Thus, with acetamide,  $\text{CH}_3.\text{CO}.\text{NH}_2$ , there is formed acetbromamide,  $\text{CH}_3.\text{CO}.\text{NHBr}$ ; these compounds are difficult to isolate on account of their ready decomposition. The paraffin amines, with halogens, exchange a hydrogen in the  $\text{NH}_2$  group. Thus, by passing chlorine into an aqueous or alkaline solution of ethylamine here is formed ethylamine dichloride,  $\text{C}_2\text{H}_5.\text{NCl}_2$ .

### B. Exchange of Halogens for One Another.

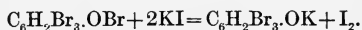
The action of chlorine on brom- and iodo-compounds does not cause a displacement of hydrogen, but an exchange of bromine or iodine for chlorine; so, in order to have chlor-brom- or chlor-iodo-compounds, it is necessary to first introduce chlorine.<sup>1</sup>

The substitution of **bromine** by **chlorine** is effected by the aid of the pentachlorides of antimony and phosphorus. Thus:



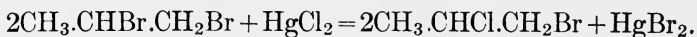
Ethylene bromide, according to the quantity of pentachloride

tion in benzene is decomposed by caustic potash, giving  $\text{C}_6\text{H}_2\text{Br}_3.\text{OH}$ . With potassium iodide it reacts according to the following equation:



<sup>1</sup> This reaction, however, may be used for obtaining chlorine substitution products: instead of allowing chlorine to act directly on the body, the liquid iodine derivatives are used, kept under water, and heated with chlorine water until liberation of iodine has ceased. In the aromatic series, only iodo-aniline,  $\text{C}_6\text{H}_4\begin{array}{c} \diagup (1) \text{NH}_2 \\ \diagdown (4) \text{I} \end{array}$  undergoes this reaction.

of antimony used, is converted into ethylene chlor-bromide,  $\text{CH}_2\text{Cl}$  or ethylene chloride,  $\text{CH}_2\text{Cl}$ ; while with methyl or ethyl-dibromides,  $\text{CH}_2\text{Br}_2$  and  $\text{CH}_3\text{CHBr}_2$ , the two bromine atoms are replaced at once. Bromine can also be replaced by heating the compound gently with mercuric chloride,  $\text{HgCl}_2$ :



**Iodine** is still more readily replaced by **chlorine**, not only by the direct action of the latter, but also by the double decomposition of an iodine compound with certain metallic chlorides, like mercuric chloride,  $\text{HgCl}_2$ , the mixture being heated in the presence of water or ether. Iodoform, under these conditions, only has two iodine atoms replaced, giving  $\text{CHICl}_2$ .

The substitution of **chlorine** by **bromine** takes place by the direct action of bromine only in the case of acid chlorides (which then behave like chloric acid, in which the chlorine is replaced by bromine), and in some other cases by double decomposition. Thus, chlor-acetic acid,  $\text{CH}_2\text{Cl.COOH}$ , heated to  $150^\circ \text{C}$ . in a sealed tube with hydrobromic acid or potassium bromide, is converted into brom-acetic acid,  $\text{CH}_2\text{Br.COOH}$ . The acid chlorides, on the contrary, under these conditions do not react: for instance, acetyl chloride,  $\text{CH}_3\text{CO.Cl}$ , heated for several hours at  $100^\circ \text{C}$ . with potassium bromide, is not changed. Aluminium bromide readily attacks alkyl chlorides; by its action, carbon tetrachloride,  $\text{CCl}_4$ , is converted into the tetrabromide,  $\text{CBr}_4$ .<sup>1</sup>

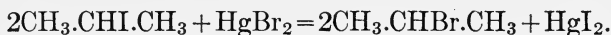
**Iodine** replaces **chlorine** when compounds of the latter (except in the aromatic series) are treated with hydriodic acid or metallic iodides  $\text{C}_6\text{H}_5\text{Cl}$  when heated with  $\text{HI}$  for fifteen hours at  $235^\circ \text{C}$ ., gives  $\text{C}_6\text{H}_6 + \text{HCl} + \text{I}_2$ .) The reaction takes place in the cold without an excess of acid. For unsaturated

<sup>1</sup> For the preparation of the halides of aluminium and their application to halogen substitution products, see Gustavsonn, *Action of the Halogen Salts of Aluminium on Organic Compounds*, Moscow, 1883 (in Russian).

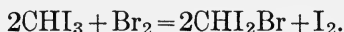
compounds, or those containing OH (which can fix HI or exchange OH), potassium iodide may be used, under  $100^{\circ}\text{C}$ . in alcoholic solution. Calcium iodide,  $\text{CaI}_2$ , may also be used (see replacement of bromine by iodine).

The best method of converting the higher chlorine derivatives into iodine compounds is to use aluminium iodide dissolved in carbon disulphide. Ethylidene chloride,  $\text{CH}_3\text{.CHCl}_2$ , becomes ethylidene iodide,  $\text{CH}_3\text{.CHI}_2$ . The trichlorhydrin of glycerol with aluminium iodide gives allyl iodide,  $\text{CH}_2=\text{CH.CH}_2\text{I}$ , together with aluminium chloride and iodine.

**Iodine** is replaced by **bromine** by the direct action of the latter, or by boiling with bromine water, or by double decomposition in a sealed tube with metallic bromides, such as those of mercury, copper, or silver. For example:



In the higher substitution products, iodine may be replaced in part or completely. Thus:



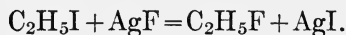
Sometimes, by the action of the hydriodic acid, there is formed an unsaturated compound which combines with the bromine. For this reason, by the action of bromine on secondary butyl iodide,  $\text{CH}_3\text{.CH}_2\text{.CHI.CH}_3$ , there is formed  $\text{CH}_3\text{.CHBr.CHBr.CH}_3$ . Iodine occurring in the aromatic nucleus, in general, is not replaceable by bromine; but the latter acting on iodo-aniline gives tribrom-aniline:



**Bromine** and **chlorine** are replaced by **iodine** by double decomposition with the iodides of potassium or calcium. The bromine compounds are heated with calcium iodide (dried with exclusion of air) in sealed tubes, generally below  $100^{\circ}\text{C}$ .

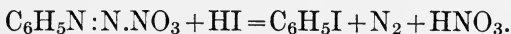
In this manner, propyl bromide,  $\text{CH}_3\cdot\text{CHBr}\cdot\text{CH}_3$ , is converted into the iodide,  $\text{CH}_3\cdot\text{CHI}\cdot\text{CH}_3$ . On account of the instability of di-iodo compounds in which the iodine occurs attached to adjoining carbon atoms, these bodies, at the moment of their formation, are decomposed into unsaturated derivatives and iodine is set free.

The substitution of **chlorine** and **iodine** by **fluorine** takes place by double decomposition of chlorine compounds with arsenic fluoride, or, in the case of iodine compounds, with silver fluoride,

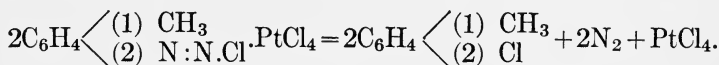


### C. The Substitution of Other Groups by Halogens.

The replacement of  $\text{NH}_2$  by a halogen is accomplished through the diazo compounds by the conversion of the  $\text{NH}_2$  into  $\text{N}:\text{N}\cdot\text{R}$ , and subsequently replacing this group with a halogen.<sup>1</sup> The halogen derivatives of the diazo bodies, such as diazo-benzene chloride,  $\text{C}_6\text{H}_5\cdot\text{N}:\text{N}\cdot\text{Cl}$ , are directly decomposed on heating, giving, in the case quoted, chlor-benzene,  $\text{C}_6\text{H}_5\text{Cl}$  and  $\text{N}_2$ . The halogen substitution products of benzene and its derivatives are also obtained by heating a diazo salt (sulphate or nitrate) with concentrated halogen acids (instead of the aqueous solution of hydrochloric acid, its acetic acid solution may be used):



The best means of preparing the chlorine substitution derivatives is to prepare the chlor-platinate of the diazo body; the precipitate is difficultly soluble in alcohol, and is collected, dried, and heated with ten times its weight of a mixture of dry soda and ground glass:

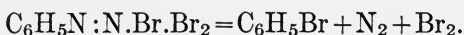


<sup>1</sup> The diazo derivatives of the aliphatic series, treated with halogens or halogen acids, have the  $\text{N}=\text{N}$  group directly replaced by a molecule of halogen or halogen acid.

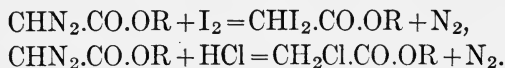
The chlor-platinates may be replaced by the double salts of the diazo-chlorides with the cuprous salts of chlorine or bromine,  $\text{Cu}_2\text{Cl}_2$  and  $\text{Cu}_2\text{Br}_2$ .

To the cold solution of the amine in dilute hydrochloric acid, there is added, little by little, the theoretical quantity of sodium nitrite, and then a solution of hydrochloric acid heated with cuprous chloride is gradually added. The double compound which is formed is generally decomposed with disengagement of nitrogen, producing the chloride and cuprous chloride, which readily separates out, owing to its insolubility.

Halogen substitution products can also be obtained by the action of halogen acids on diazo-amido compounds. This is the best means of preparing iodine and fluorine compounds. Thus, benzene fluoride,  $\text{C}_6\text{H}_5\text{F}$ , is prepared by the action of hydrofluoric acid on  $\text{C}_6\text{H}_5\text{N:N.NC}_5\text{H}_{10}$ . The latter body is produced by the action of diazobenzene chloride on piperidine. For preparing bromine compounds there may be utilized the decomposition of the perbromides, which are formed by the action of bromine in hydrobromic acid solution on an aqueous solution of the diazo sulphate. The compound is washed with alcohol and dried. On heating, alone or with glacial acetic acid, it is decomposed according to the equation:



The substitution of the  $-\text{N}=\text{N}-$  group by halogens or halogen acids takes place by the action of these on the diazo compounds of the aliphatic series. Thus, diazo-acetic-ester gives di-iodo-acetic-ester with iodine in alcoholic solution and at the ordinary temperature;<sup>1</sup> by the action of hydrochloric acid it gives chlor-acetic ester.




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<sup>1</sup> Titration with iodine is used in the quantitative determination of the diazo compounds of the aliphatic series.

**Substitution of OH by a halogen.**—The alcoholic OH group is replaced by halogens on treatment with a concentrated halogen acid, or with a mixture which liberates such acids (NaCl and H<sub>2</sub>SO<sub>4</sub>; KBr and H<sub>2</sub>SO<sub>4</sub>).

With hydrochloric acid the action is quite slow, and heat is generally required to bring about the reaction, either in a sealed tube or in the presence of dehydrating agents. Hydrobromic acid reacts more easily, and hydriodic acid still more so, and in the latter case it is not always necessary to use heat. Instead of acids, bromine or iodine may also be allowed to act on the alcohols in the presence of phosphorus.

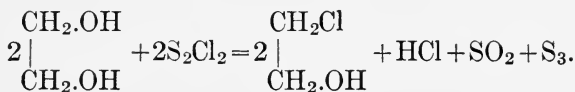
It must not be forgotten that an excess of acid may act as a reducing agent.<sup>1</sup> In certain cases this reaction takes place more easily than that of replacing OH by I. Thus, iod-acetic acid, CH<sub>2</sub>I.CO.OH, reacts in the cold, even with sufficiently diluted hydriodic acid; while glycollic acid, CH<sub>2</sub>(OH).CO.OH, only reacts when heated with concentrated acid. This is why iod-acetic acid is not formed by the action of hydriodic acid on glycollic acid. Lactic acid behaves in the same manner, which distinguishes it from the iosmeric hydraerylic acid, CH<sub>2</sub> $\begin{matrix} \diagup \text{CH}_2\text{OH} \\ \diagdown \text{CO.OH} \end{matrix}$ , which readily forms an iodide.

Compounds rich in hydroxyl, with hydriodic acid, readily exchange one or more of their OH groups for H, by reason of the reaction of the acid with the iodo product: thus, with glyceric acid is obtained  $\beta$ -iodo-propionic acid, CH<sub>2</sub>I.CH<sub>2</sub>.CO.OH; the iodine which occurs in the primary group is always the more stable. In polyatomic alcohols, on the contrary, the iodine which is found in the secondary group (called beta) shows the greater stability. If in the compound there are several hydroxyl groups, according to the conditions of the experiment, it is possible to replace all or some of them with chlorine. For an incomplete exchange, there may be used, among others, sulphur chloride, S<sub>2</sub>Cl<sub>2</sub>, which reacts,<sup>2</sup> for exam-

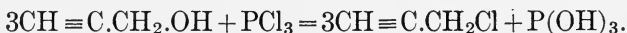
<sup>1</sup> See substitution of iodine by hydrogen.

<sup>2</sup> The product obtained always contains sulphur.

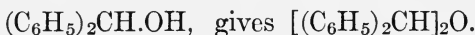
ple, with glycol, according to the equation:



Instead of using the halogen acids, the different halogen compounds of phosphorus may be used, which react with great energy. In certain bodies, as, for example, phenols, carboxylic, and sulphonic acids, it is only by this means that OH may be exchanged for a halogen.<sup>1</sup> The trichloride of phosphorus is used in cases where other reactions than the exchange of OH may take place, such as the fixation of hydrochloric acid. Propargyl alcohol reacts according to the following equation:



Sometimes the action of the trichloride leads to the formation of anhydrides, as with benzhydrol:



The pentachloride is usually applied in cases where the body contains several hydroxyl groups and it is necessary to replace them all; erythrite, for example, gives erythrene tetrachloride,  $\text{C}_4\text{H}_6\text{Cl}_4$ . The pentachloride and pentabromide of phosphorus are used for the replacing of OH by Cl and Br in phenols and in carboxylic and sulphonic acids. In aliphatic acids, the same result is gained by the action of  $\text{PCl}_3$  or  $\text{POCl}_3$ .<sup>2</sup>

<sup>1</sup> The OH of carboxylic acids may be replaced by chlorine with hydrochloric acid only in the presence of phosphoric anhydride. Thus, by passing a current of the gas into glacial acetic acid mixed with  $\text{P}_2\text{O}_5$ , acetyl chloride is formed even at  $0^\circ\text{C}$ . But benzoyl chloride can only be obtained by passing hydrochloric acid gas into a mixture of benzoic acid and  $\text{P}_2\text{O}_5$  heated to  $200^\circ\text{C}$ .

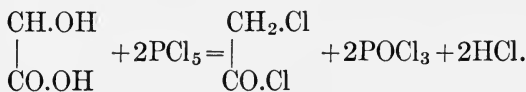
<sup>2</sup> For the preparation of the acid bromides, in place of  $\text{PBr}_3$ , it is more convenient to use a mixture of the acid with phosphorus, while bromine is added from time to time in quantity corresponding to the equation:





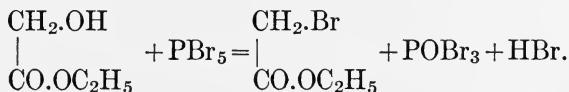
By the action of  $\text{PCl}_5$  on the oxy-acids, the hydroxyl groups are replaced by Cl. The aromatic oxy-acids at first give combinations which contain phosphorus and chlorine like

$\text{C}_6\text{H}_4 \begin{array}{c} \diagup \text{CO} \diagdown \\ \diagdown \text{O} \diagup \end{array} \text{PCl}_3$ , which finally become, by the action of the pentachloride or simply by the action of heat, chlorinated acid chlorides,  $\text{C}_6\text{H}_4 \begin{array}{c} \diagup \text{COCl} \diagdown \\ \diagdown \text{Cl} \diagup \end{array}$ . Glycollic acid gives chlor-acetylchloride, according to the following equation:

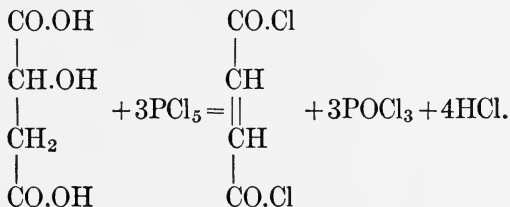


The same reaction takes place with the perbromide.

In order to obtain a brom derivative of an oxy-acid, it is necessary to heat the latter with hydrobromic acid, or to use the perbromide with the ether of the oxy-acid. Thus:



With certain polybasic oxy-acids there are formed unsaturated derivatives of the acids: thus, malic acid gives fumaryl chloride: tartaric acid is converted into chlor-malyl chloride:

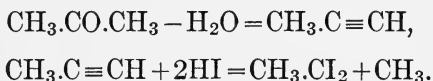


**Replacing a halogen by OH.** (See Chapter on Oxidation.)

The replacing of O in the CO group of aldehydes, ketones, ketonic acids, and other compounds by Cl or Br is done by

using the perchloride or perbromide (it is better to take the chlor-bromide, because it is easier to separate the oxychloride by oxidation). The reaction takes place in the cold; often it is necessary to moderate the temperature by cooling, or by addition of oxychloride; in certain cases it is necessary to heat either under ordinary pressure or in sealed tubes. During this reaction the halogen acid is sometimes disengaged.

The replacing of O by I<sub>2</sub> cannot be done directly. It is necessary to operate indirectly by first splitting off water, then treating with hydriodic acid, which is then fixed by the unsaturated body:

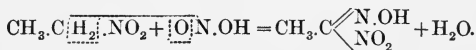


#### D. Preparation of the Derivatives of Nitrous and Nitric Acids and of Hydroxylamine.

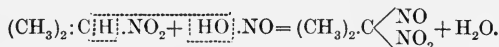
**Replacing H by NO.**—The introduction of the NO group by the substitution of hydrogen linked to a carbon atom only takes place in a few cases. It is believed that this reaction occurs when mixture of potassium nitrite and sulphuric acid is allowed to act on an alkaline solution of secondary nitro compounds, such as nitro-isopropane, (CH<sub>3</sub>)<sub>2</sub>CH.NO<sub>2</sub>, which is converted into isopropyl-pseudonitrol, (CH<sub>3</sub>)<sub>2</sub>C(NO)NO<sub>2</sub>.<sup>1</sup>

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<sup>1</sup> Nitro compounds are differently affected by nitrous acid, according to whether they are primary, R.CH<sub>2</sub>.NO<sub>2</sub>, secondary, R<sub>2</sub>:CH.NO<sub>2</sub>, or tertiary, R<sub>3</sub>:C.NO<sub>2</sub>. Primary nitro compounds are converted into *nitrolic acids* (oximid-compounds) which dissolve in alkalis with an intense *red* color:



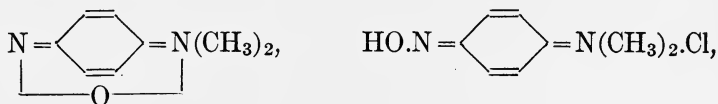
Secondary nitro compounds give *pseudo-nitrols*, which are soluble in alkalis, giving a deep *blue* color:



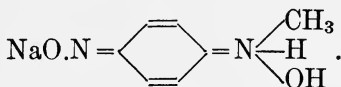
Tertiary nitro compounds do not react with nitrous acid. These reactions afford a delicate method of detecting primary, secondary, and tertiary alcohols; the alcohols are first converted into iodides (with PI<sub>3</sub>), and then treated with

Certain aromatic tertiary bases, such as dimethyl-aniline,  $\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_2$ , are changed into nitroso derivatives by the theoretical amount of potassium nitrite or amyl nitrite added to their hydrochloric acid solutions, well cooled. This reaction does not appear to be general; for the *ortho*- and *para*-dimethyl-toluidines do not form nitroso derivatives, while the *meta*-body furnishes  $\text{C}_6\text{H}_3(\text{NO})(\text{CH}_3)\text{N}(\text{CH}_3)_2$ . It is possible that this may not be a nitroso compound, but an isonitroso compound.

The nitroso-amines of the aromatic bases are converted into para-nitroso derivatives, similar to para-nitroso-dimethyl-aniline, by an alcoholic solution of hydrochloric acid. It is thought by some that nitroso-dimethyl-aniline may be an azoxy derivative and may have the quinonoid formula



which would explain the formation of the sodium salt of para-nitroso-monomethyl-aniline:



The other aromatic derivatives either do not react with nitrous acid, or behave in quite a different manner. Thus, with phenol, there is formed a body which for long was considered as nitroso-phenol, but which is really a quinone-oxime. Perhaps it is formed as an isomeride of the isonitroso compound

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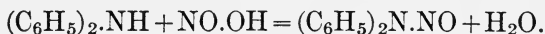
silver nitrite ( $\text{AgNO}_2$ ). The nitro compounds which are thus formed are distilled off and mixed with potassium nitrite and sulphuric acid; on adding an excess of potassium hydrate the liquid becomes either red or blue, or remains unchanged, according to whether the alcohol was primary, secondary, or tertiary. Only the alcohols of low molecular weight show these color reactions.

which may at first be produced:



Nitrous acid with alcohols of the aliphatic series simply replaces the hydrogen of the alcoholic group to form nitrous esters. These are easily obtained by saturating the alcohol with  $\text{N}_2\text{O}_3$ , and the reaction, if necessary, is completed by the aid of heat; or, better, to a mixture of the alcohol with sulphuric acid and water, there is added a solution of potassium nitrite, and the ester formed is subsequently isolated. A very convenient method for preparing these esters is to employ the double decomposition between the alcohols and the nitrous ester of glycerine.<sup>1</sup>

The hydrogen united to the nitrogen of imido compounds is easily replaced by NO by the action of nitrous acid; in this manner are formed the nitrosamines:



These nitrosamines are prepared by passing  $\text{N}_2\text{O}_3$  into a solution of the imide base (in alcohol, ether, benzene, acids, etc.). The body produced is separated by evaporating the solution or by diluting with water. There may also be used potassium nitrite, which is added in the theoretical quantity to a hydrochloric acid solution of the base; or the nitrous esters of ethyl and amyl alcohol may be employed.

The anilides behave in the same manner, but the nitroso bodies formed are distinguished from the nitrosamines by their instability. Nitroso-anilide,  $(\text{C}_6\text{H}_5)(\text{CH}_3.\text{CO})\text{N.NO}$ , is prepared by passing  $\text{N}_2\text{O}_3$  into a solution of the anilide in glacial acetic acid. Piperidine and its derivatives (for example, conine or  $\alpha$ -propyl-piperidine) and tetrahydro-quinoline also give nitroso compounds.

<sup>1</sup> *Gaz. chim. ital.*, vol. 15, p. 351.

**Substitution of H by NO<sub>2</sub>.**—This substitution only takes place easily in the aromatic series by the action of nitric acid. In the aliphatic series nitro compounds are rarely formed. Mention, however, may be made of the formation of C(NO<sub>2</sub>)<sub>4</sub>, nitro-isobutylene, and nitro-barbituric acid; it may also be remarked that nitro-styrene probably has the formula C<sub>6</sub>H<sub>5</sub>.CH:CH.NO<sub>2</sub>. Further mention will be made of those compounds, known as dinitroso, obtained by the action of nitric acid on ketones.

In the aromatic series, nitration is a very general one. In order to nitrate the aromatic hydrocarbons, they are added little by little to fuming nitric acid, and it is better that the latter does not contain any nitrogen oxides; or the acid may be added slowly to the hydrocarbon. A sufficient quantity of water is added to isolate the nitro derivative. It is often easier to regulate the nitration by operating with a glacial acetic acid solution. The nitric acid employed in the majority of cases has a density of 1.50 to 1.52.<sup>1</sup> In the nitration of benzene, an excess of benzene diminishes the yield of nitrobenzene, an excess of acid increases it.

Nitration in general does not have to be made at elevated temperatures; it is often necessary to use refrigeration, sometimes to 0° C., for nitric acid also acts as an oxidizing agent; and, if the hydrocarbons have side-chains, they may be converted into carboxylic acids or ketones. The ease of nitration increases with the number of side-chains. In order to obtain higher nitro products, the reaction is carried out with a mixture of nitric and sulphuric acids, or with the aid of heat, if necessary. The sulphonic acid compounds, if heated strongly during nitration, may have their SO<sub>3</sub>H group replaced. Thus, mesitylene sulphonic acid, C<sub>6</sub>H<sub>2</sub>(CH<sub>3</sub>)<sub>3</sub>SO<sub>3</sub>H, if it is not cooled, gives dinitro-mesitylene, C<sub>6</sub>H(NO<sub>2</sub>)<sub>2</sub>(CH<sub>3</sub>)<sub>3</sub>.

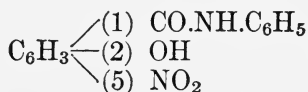
The nitro-sulphonic acids, being soluble in water, cannot

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<sup>1</sup> For the action of nitric acid of different concentrations on the aromatic hydrocarbons and their derivatives, see *Annalen*, vol. 224, p. 283.

be separated by addition of the latter; in order to accomplish this, the acid liquor is diluted with a little water and the excess of nitric acid is evaporated off on a water-bath.

Phenols are nitrated so easily that it is not necessary to use fuming nitric acid. Phenolic ethers behave in the same manner. The amido compounds<sup>1</sup> react readily with nitric acid, and give at once higher nitro products, or even resinous matters; also it is only necessary to use the theoretical quantity of acid or to employ it dilute. With aniline, for example, the amine is dissolved in a large quantity of cold sulphuric acid, and there is added, little by little, a mixture of the theoretical quantity of nitric acid with sulphuric acid. When the reaction is finished, the mass is diluted with water, and the excess of acid neutralized in order to precipitate the nitro-amido compound. In the majority of cases the amido compound itself is not nitrated, but the anilide; the reaction proceeds nicely, and, according to the concentration of the acid, either mono- or dinitro products can be obtained. The NO<sub>2</sub> group always replaces the hydrogen in the benzene nucleus of the base, even in the case where the anilide contains the residue of an aromatic acid. The anilides of the oxy-benzoic acids offer an exception; in the nitration of salicyl anilide,  $\text{C}_6\text{H}_4 \begin{matrix} \swarrow (1) \text{CO.NH.C}_6\text{H}_5 \\ \searrow (2) \text{OH} \end{matrix}$ , the principal product obtained is



The nitro-anilides, on saponification, by heating with a concentrated halogen acid or with caustic soda, yield the nitro-amido compounds. (To obtain the nitro compounds by the reduction of the dinitro derivatives, see under Chapter II.)

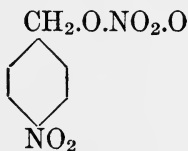
The carboxylic acids are nitrated less easily. Containing side-chains, they should be nitrated cold, or by using a less con-

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<sup>1</sup> For the production of the nitro-dimethylanilines, see under Chapter I.

centrated acid. The oxy-carboxylic acids, like the acid phenols, are nitrated very readily; salicylic acid, with fuming nitric acid, immediately gives a dinitro acid; to obtain the mono-nitrated acid, it is necessary to dilute the nitric acid with glacial acetic acid. The aldehydes and ketones require to be cooled considerably; they are nitrated by using a mixture of nitric and sulphuric acids. Quinoline and its derivatives only have the hydrogen of the benzene nucleus replaced, and not that of the pyridine, by the action of nitric acid.

The formation of nitric esters by the action of nitric acid on alcohols gives rise to the substitution of the hydrogen in hydroxyl by  $\text{NO}_2$ . Though frequent in the aliphatic series, this reaction is rare in the aromatic compounds. The nitric acid used has a density of 1.3 to 1.4, and is deprived of its nitrous vapors by urea; it is cooled and mixed with the alcohol. The ester formed is separated by distillation or addition of water. If the alcohol reacts with difficulty, heat is used, or sulphuric acid. It is necessary to avoid the formation of reddish-brown nitrous fumes. Many oxy-acids behave in the same manner as the alcohols. Among the aromatic alcohols, the only one which yields a nitric acid ester is para-nitro-benzyl alcohol:



**Replacement of  $\text{NH}_2$  by  $\text{NO}_2$ .**—This can be brought about by the use of the diazo compounds, for which purpose the nitrous salts are treated with copper suboxide. For example, the nitrite of diazo-benzene,  $\text{C}_6\text{H}_5\text{N}:\text{N}.\text{O}.\text{NO}$ , gives nitro-benzene,  $\text{C}_6\text{H}_5.\text{NO}_2$ , with liberation of  $\text{N}_2$ . The amido compound is dissolved in two molecules of nitric acid, or in one molecule of dilute sulphuric acid; and there is added one molecule of alkaline nitrite, then a second molecule to form the

salt. To the solution is now added some copper suboxide; there is a disengagement of nitrogen and a formation of the nitro compound.

**Substitution of a halogen by an  $\text{NO}_2$  Group.**—This is about the only method of obtaining the nitro derivatives of the aliphatic series, and it is effected by allowing  $\text{C}_n\text{H}_{2n+1}\text{I}$  to react with  $\text{AgNO}_2$  or  $\text{KNO}_2$ . However, it cannot as yet be affirmed with certainty that the compounds obtained are true nitro derivatives.<sup>1</sup> These are not the only bodies formed, however, as simultaneously there are always produced more or less isomeric nitrous esters.<sup>2</sup> The more hydrogen there is attached to the carbon atom holding the iodine, the less will be the quantity of nitrous ester produced; thus, methyl iodide,  $\text{CH}_3\text{I}$ , furnishes only nitro-methane. Ethyl iodide gives partly nitrous ester and partly nitro-ethane; and, finally, tertiary isobutyl iodide,  $(\text{CH}_3)_3\text{CI}$ , forms only a small quantity of nitro-butane. In certain cases the unsaturated hydrocarbons are produced as secondary products, as in the reaction of silver nitrite on secondary butyl iodide,  $\text{CH}_3\cdot\text{CH}_2\cdot\text{CHI}\cdot\text{CH}_3$ , where butylene is disengaged. It is very seldom that iodine compounds are distinguished from those of bromine. The reaction, especially at the beginning, takes place with much energy, so that it is prudent to introduce the silver nitrite in small quantities at a time, and to keep the vessel containing the mixture well cooled. Under these conditions about 66 per cent of nitro-ethane can be obtained.<sup>3</sup>

The separation of the nitro derivatives and the isomeric nitrous esters offers no great difficulty, the latter being the more volatile. They may also be separated by the addition of alcoholic soda; for the nitro compounds, with the exception of the tertiary ones, form sodium compounds which are

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<sup>1</sup> See *Jour. Soc. Phys. Chim. Russe*, vol. 18, p. 385.

<sup>2</sup> In this there is a difference between the reactions  $\text{RI} + \text{MNO}_2$  and that of  $\text{RI} + \text{MSO}_3\text{H}$ ; for, in the latter case, sulphonic acids are almost exclusively obtained, without the formation of isomeric esters, as in the case of the nitro derivatives.

<sup>3</sup> See *Jour. Soc. Phys. Chim. Russe*, vol. 14, p. 227.



difficultly soluble. During the reaction of iodo-ethyl alcohol,  $\text{CH}_2\text{I}.\text{CH}_2.\text{OH}$ , with silver nitrite, there is formed some nitro-ethyl alcohol,  $\text{CH}_2.\text{NO}_2.\text{CH}_2.\text{OH}$ . But iodo-ethylene and chlor-iodo-ethylene do not react completely with silver nitrite, and dinitro compounds are not produced.

The dinitro compounds are formed by the action of potassium nitrite on brom-nitro derivatives. For example, to the alcoholic solution of brom-nitro-ethane,  $\text{CH}_3.\text{CHBr}.\text{NO}_2$ , there is added an aqueous solution of potassium nitrite, and then an alcoholic solution of alkali; there is formed the body  $\text{CH}_3.\text{CK}(\text{NO}_2)_2$ , which, on treatment with sulphuric acid, gives dinitro-ethane,  $\text{CH}_3.\text{CH}(\text{NO}_2)_2$ .

Some of the nitro compounds are seemingly obtained by the action of nitric acid on the substituted aceto-acetic esters, and on secondary alcohols (isopropyl alcohol excepted). Some chemists do not consider these bodies as nitro compounds, but as nitrous esters of dihydrates. Thus the nitro-propane compound,  $\text{CH}_3.\text{CH}_2.\text{CH}(\text{NO}_2)_2$ , is given the formula  $\text{CH}_3.\text{CH}_2.\text{CH}(\text{ONO})_2$ . The formation of the potassium salts (yellow crystals) of the dinitro compounds, or nitrous acid esters, is a characteristic reaction for secondary alcohols.<sup>1</sup>

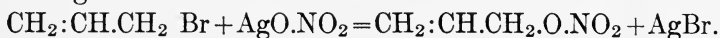
Iodo-benzene,  $\text{C}_6\text{H}_5\text{I}$ , with silver nitrite, reacts when heated for a long time, and gives nitro derivatives of phenol. With benzyl iodide,  $\text{C}_6\text{H}_5\text{CH}_2\text{I}$ , there is formed benzaldehyde, benzoic acid, and nitrous oxide,  $\text{NO}$ .

In certain cases the halogen of carboxylic acids can also be replaced by  $\text{NO}_2$ . Thus brom-ethyl acetate,  $\text{CH}_2\text{Br}.\text{CO}.\text{OC}_2\text{H}_5$ , with silver nitrite, gives ethyl nitro-acetate,  $\text{CH}_2\text{NO}_2.\text{CO}.\text{OC}_2\text{H}_5$ ; even  $\beta$ -brom-propionic acid,  $\text{CH}_2.\text{Br}.\text{CH}_2\text{CO}.\text{OH}$ , is converted into  $\beta$ -nitro-propionic acid. With chlor-acetic acid,  $\text{CH}_2\text{Cl}.\text{CO}.\text{OH}$ , and potassium nitrite, in place of nitro-acetic acid, there are produced decomposition products of  $\text{CH}_3\text{NO}_2$  and  $\text{CO}_2$ .

**Substitution of a halogen by  $\text{O}.\text{NO}$ .**—Formation of nitrous esters from  $\text{RI}$  and  $\text{MNO}_2$ . (See page 88.)

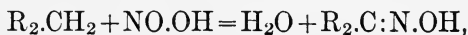
<sup>1</sup> This is Chancel's reaction. See *Bull. Soc. Chim.*, vol. 31, p. 504, and *Compt. rend.*, vol. 100, p. 604.

**Substitution of a halogen by  $\text{O.N.O}_2$ .**—Formation of nitric esters by the action of silver nitrate on halogen compounds. The nitric ester of allyl alcohol is obtained according to the following reaction:

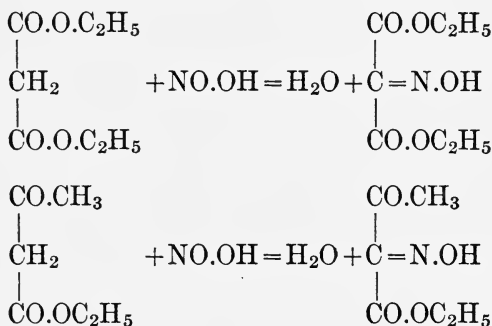


In the same way, para-nitro-benzyl chloride,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{CH}_2\text{Cl} \\ \text{NO}_2 \end{smallmatrix}$ , with silver nitrate, gives  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{CH}_2.\text{O.N.O}_2 \\ \text{NO}_2 \end{smallmatrix}$ .

**Substitution of  $\text{H}_2$  by  $>\text{N.OH}$ .**—When nitrous acid acts on bodies which contain a  $\text{CH}_2$  group (adjoining negative groups such as  $\text{CO}$  or  $\text{NO}_2$ ), the following reaction takes place:

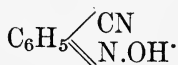


and isonitro compounds are formed, thus:



In order to obtain isonitroso-malonic ester,  $\text{N}_2\text{O}_3$  is passed into a mixture of malonic ester and sodium alcoholate until no further absorption takes place; the isonitroso compound is separated by the addition of water. In order to obtain isonitroso-aceto-acetic ester, potassium nitrite is added to a solution of aceto-acetic ester in an alkaline alcoholic mixture, while it is well cooled, and then 20 per cent. sulphuric acid is run in. After the reaction is completed the liquid is made alkaline, and any unchanged aceto-acetic ester is removed by ether; on acidifying again, the isonitroso compound is separated.

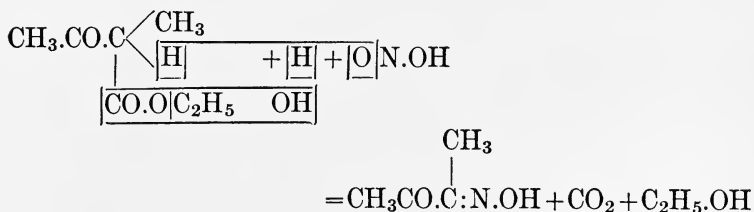
Benzyl cyanide,  $\text{C}_6\text{H}_5\cdot\text{CH}_2\cdot\text{CN}$ , with amyl nitrite in the presence of alcohol, is also converted into an isonitroso compound,



The substituted aceto-acetic esters of the general formula

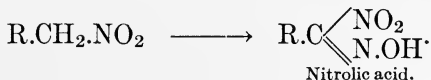


during their transformation into isonitroso compounds, are saponified at the same time, and the final reaction may be expressed thus:



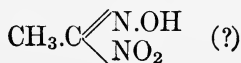
The isonitroso ketones may be obtained by treating ketones with amyl nitrite in the presence of hydrochloric acid or sodium ethylate.

Primary nitro compounds (or rather their metallic salts) are converted into nitrolic acid derivatives (the salts) by nitrous acid. It is supposed that  $\text{H}_2$  is exchanged for  $>\text{N.OH}$ .

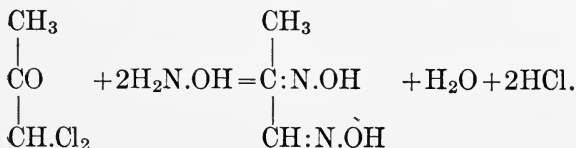


During the formation of diazo compounds, there also occurs the substitution of  $\text{H}_2$  (of the amido group) by  $>\text{N.OH}$  (or  $>\text{NCl}$ ,  $>\text{N.NO}_3$ , etc.).

**Substitution of a halogen by  $\text{N.OH}$**  takes place in the action of hydroxylamine on compounds which contain two atoms of halogen attached to a single carbon atom. Dibrom-nitro-ethane,  $\text{CH}_3\cdot\text{CBr}_2\cdot\text{NO}_2$ , is presumably converted into ethyl nitrolic acid,

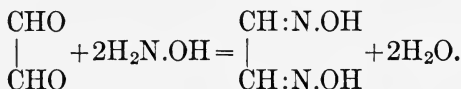


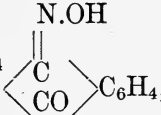
The halogen substitution products of ketones behave in the same manner; but their oxygen also reacts with hydroxylamine and produces oximido ketoximes;



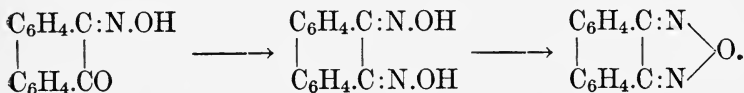
**Substitution of O by N.OH.**—Aldehydes and ketones, as well as quinones, replace the O by N.OH by the action of hydroxylamine in aqueous or alcoholic solution, giving rise to aldoximes, ketoximes, and quinone-oximes. The reaction proceeds tranquilly in the cold by leaving the two bodies in contact. It is more convenient to use a solution of hydroxylamine hydrochloride (the presence of ammonium chloride is not injurious) with the theoretical quantity of sodium carbonate.

Ketonic or aldehydic acids and their esters readily react with hydroxylamine. Bodies which contain two CHO or CO groups react with two and sometimes with only one molecule of hydroxylamine. Glyoxal gives glyoxime:



The oxime obtained with anthraquinone,  $\text{C}_6\text{H}_4$    $\text{C}_6\text{H}_4$ ,

does not react any further with hydroxylamine, while its isomer, prepared with phenanthraquinone, reacts at 180° C. with another molecule of hydroxylamine, giving the dioxime or its anhydride:



The oxime, which corresponds to benzoquinone, and which is para-nitroso-phenol, obtained by the action of hydroxylamine on quinone, reacts with another molecule, giving quinone-dioxime,  $C_6H_4(N.OH)_2$ .

### E. Preparation of Ammonia Derivatives.

**Substitution of a halogen by  $NH_2$ .**—In the aliphatic series, and in the side-chains of the aromatic series, this takes place through the action of ammonia on the halogen esters. However, the reaction cannot be expressed by the simple equation  $RI + 2NH_3 = RNH_2 + NH_3.HI$ , because, besides the primary amines, there are also produced secondary amines, according to the time, the temperature, and the mass of the reacting bodies.<sup>1</sup>

It is also necessary to take into consideration whether aqueous or alcoholic solutions of ammonia are used, and also the character of the halogen compounds. In the case of primary compounds, there are formed not only tertiary amines but also ammonium derivatives; in the case of secondary bodies, the chief product consists of primary bases. The tertiary iodides react with ammonia but do not give amines; they are decomposed with the formation of unsaturated hydrocarbons.<sup>2</sup> The reaction is carried out in sealed tubes at  $100^\circ C$ .<sup>3</sup>

The separation of the primary amines from the products formed with them is sometimes very difficult. With the lower homologues, recourse cannot be had to distillation, as the difference between the boiling-points of the primary, secondary, and tertiary amines is too small. Generally, recourse is had to the oxalic esters. The product of the reaction

<sup>1</sup> According to some, these bodies are formed successively; and, as there is always an excess of ammonia, the free bases are produced, their alkalinity being more feeble than that of ammonia, which decomposes their salts.

<sup>2</sup> Also, during the reaction of secondary iodides with ammonia and the amines, the unsaturated hydrocarbons are readily formed. Isopropyl iodide,  $(CH_3)_2CHI$ , with isopropylamine,  $(CH_3)_2CH.NH_2$ , gives propylene,  $CH_3.CH : CH_2$ .)

<sup>3</sup> Methylamine can be formed at the ordinary temperature by liquefying a mixture of methyl chloride and ammonia.

is evaporated on a water-bath, then potash is added to the mixture of the salts, and on distillation the ammonium compound, is left behind, as it is not decomposed by potash. The distillate consists of the amines  $R.NH_2$ ,  $R_2.NH$ , and  $R_3.N$ . This mixture of amines is then treated by the oxalic ester method.

The aromatic amines may be separated by the fractional crystallization of their salts; the salts of the secondary amines are less soluble than those of the primary, and more so than those of the tertiary. Also the difference in basicity is utilized, and the separation may be accomplished by means of acids. Thus, a mixture of benzylamines, taken up with a small quantity of dilute hydrochloric acid, will give up at first the mono- and di-benzylamines,  $(C_6H_5.CH_2).NH_2$  and  $(C_6H_5.CH_2)_2.NH$ , and these may be separated subsequently by crystallization; the residue will be the tertiary amine,  $(C_6H_5.CH_2)_3.N$ .

The halogen of chlorhydrins,  $(CH_2.Cl.CH_2OH)$ , as well as the substitution products of the carboxylic acids, may also be replaced by  $NH_2$ . The ester of chlor-formic acid,  $ClCO.OR$ , with ammonia, gives carbamic acid,  $NH_2CO.OR$ . The esters of other chlor-acids behave in a slightly different manner; they are converted into chlor-acid amides. With chlor-ethyl

acetate,  $\begin{array}{c} CH_2Cl \\ | \\ CO.OC_2H_5 \end{array}$ , there is formed chlor-acetamide,  $\begin{array}{c} CH_2Cl \\ | \\ CO.NH_2 \end{array}$ ,

which, heated with ammonia, has the chlorine replaced to give amido-acetamide,  $NH_2CH_2.CO.NH_2$ . For the preparation of similar amines, heating with lead hydrate is employed; the lead salt thus obtained is decomposed by means of hydrogen sulphide.

The other esters of the inorganic acids behave in the same manner as the halogen compounds.

In the aromatic nucleus the halogen is seldom replaced by the amido group by treatment with ammonia. Brom-nitrobenzene,  $C_6H_4 \begin{array}{l} \swarrow (1) NO_2 \\ \searrow (2) Br \end{array}$ , and similarly chlor-nitrobenzene,

$C_6H_4$   $\begin{matrix} \swarrow (1) \text{ Cl} \\ \searrow (4) \text{ NO}_2 \end{matrix}$ , heated in sealed tubes at  $180^\circ \text{ C.}$  with ammonia, give nitraniline; but the meta-brom-nitrobenzene scarcely reacts at all with ammonia. In chlor-dinitrobenzene,

$C_6H_3$   $\begin{matrix} \swarrow (1) \text{ Cl} \\ \searrow (2) \text{ NO}_2 \\ \searrow (4) \text{ NO}_2 \end{matrix}$ , the chlorine is replaced by simply boiling

with ammonia water. The corresponding bromine compound reacts with difficulty, and the iodine compound is even less reactive. If two  $\text{NO}_2$  groups are found in the ortho position to one another, one of the two can be replaced by  $\text{NH}_2$ .

Thus chlor-dinitrobenzene,  $C_6H_3$   $\begin{matrix} \swarrow (1) \text{ Cl} \\ \searrow (3) \text{ NO}_2 \\ \searrow (4) \text{ NO}_2 \end{matrix}$ , is converted into

chlor-nitrotoluidine,  $C_6H_3$   $\begin{matrix} \swarrow (1) \text{ Cl} \\ \searrow (3) \text{ NH}_2 \\ \searrow (4) \text{ NO}_2 \end{matrix}$ .

The substitution of halogens by  $\text{NH}_2$  takes place easily by the action of aqueous or gaseous ammonia on the chlorides of the carboxylic acids. The reaction takes place in the cold and gives very good yields. In the aliphatic series there is also formed a secondary amine as a by-product. In carrying out the reaction, the acid and phosphorus trichloride are taken, and not the ready-prepared chloride.

By cautiously treating with ammonia such compounds as dichlor-propionyl chloride,  $\text{CH}_3.\text{CCl}_2.\text{CO}.\text{Cl}$ , the chlorine is only replaced in the  $\text{COCl}$  group.

The chlorides of the sulphonic acids react with difficulty; their amides can be prepared, nevertheless, by using gaseous ammonia dissolved in ether, and, less readily, by prolonged boiling with aqueous ammonia.

**Substitution of  $\text{OH}$  by  $\text{NH}_2$ .**—This can only be effected by heating with ammonia or its salts in sealed tubes, with or without dehydrating agents. With the aliphatic alcohols there are formed primary, secondary, and tertiary amines, and often, as by-products, unsaturated hydrocarbons. One may conveniently use the ammoniacal chloride of zinc, which

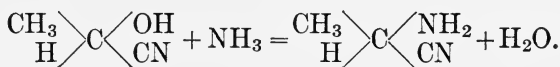
is prepared by passing ammonia over powdered zinc chloride heated to 300° C. The latter absorbs four times its weight of ammonia. The body R.OH is heated for fifteen hours at 250° C. with the ammoniacal chloride. The yield is from 50 to 75 per cent. of the weight of the alcohol used in the reaction.

The reaction with phenols takes place more readily.  $\beta$ -naphthylamine, with a certain quantity of  $\beta$ -dinaphthylamine, is obtained by passing dry ammonia over  $\beta$ -naphthol strongly heated. Anthrol gives anthramine:



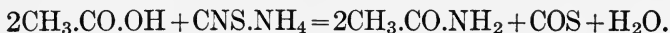
When heated to 200° C. with aqueous ammonia, alizarin is converted into diamido anthraquinone. Many of the nitrophenols also react readily with ammonia in concentrated solution. With other phenols, ordinary phenol for example, it is necessary to heat with ammoniacal chlorides of zinc or calcium at elevated temperatures. One part of the phenol remains unattacked; but it is easy to separate this from R.NH<sub>2</sub> by the aid of acids and alkalies.

The cyan-hydrins (produced by the combination of hydrocyanic acid with aldehydes and ketones) react with ammonia with remarkable ease, and give the nitriles of the  $\alpha$ -amidocarboxylic acids. Thus:



The latter body, on saponification, gives amido-propionic acid or alanine.

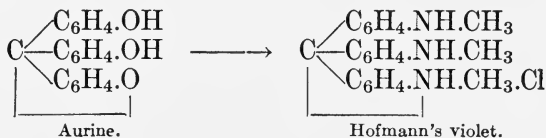
The acids of the aliphatic series have their OH replaced by NH<sub>2</sub>, and are converted into amides, when they are treated with ammonium sulphocyanide, CNS.NH<sub>4</sub>:





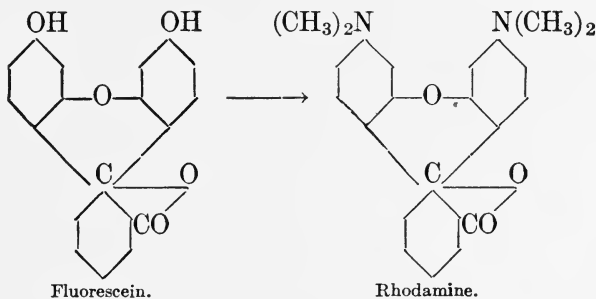
There is generally formed a certain quantity of nitrile as a secondary product.

**Substitution of OH by NH.R and NR<sub>2</sub>.**—This is accomplished by heating phenolic bodies with primary and secondary amines, NH<sub>2</sub>.R and NH.R<sub>2</sub>. The reaction is sometimes more easily brought about than with ammonia. Thus aurine is more readily converted into trimethyl-rosaniline than into rosaniline:



$\alpha$ - and  $\beta$ -naphthols are converted into monomethyl  $\alpha$ - and  $\beta$ -naphthylamines by the action of monomethylamine.

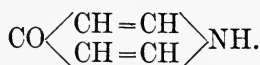
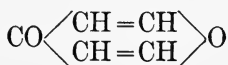
Fluorescein heated with dimethylamine gives tetramethyl-diamido-fluorescein, or rhodamine, a magnificent red dyestuff:



These cases can be considered as indirect condensations with disengagement of water.

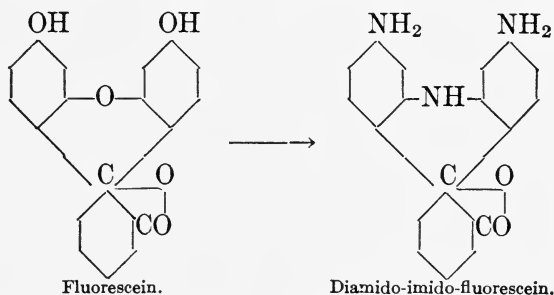
**Substitution of O by NH.**—This is brought about in certain cases by the action of ammonia. Thus, different derivatives of pyrone, C<sub>5</sub>H<sub>4</sub>O<sub>2</sub>, heated with ammonia, and sometimes even at the ordinary temperature, are converted into pyridone derivatives, C<sub>5</sub>H<sub>4</sub>O.NH. The acid C<sub>5</sub>H<sub>3</sub>O<sub>2</sub>, CO.OH, .

forms  $C_5H_4O.N.CO:OH$ . The following formulas represent pyrone and pyridone:

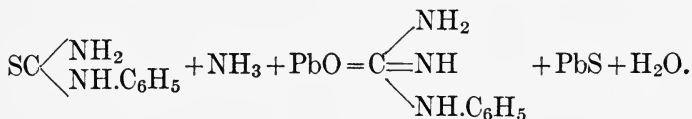


As derivatives of pyrone, there are, among others, meconic acid, chelidonic acid, which is tribasic, and pyromeconic acid, which probably does not contain a carboxyl group, but which should be hydroxypyrene,  $C_5H_3(OH)O_2$ .

On heating fluorescein with ammonia there is substituted not only  $OH$  by  $NH_2$ , but also  $O$  by  $NH$ . The following formulas for these bodies have been given:



**Substitution of S by NH.**—When sulphur is attached to a carbon atom with two bonds, it may be replaced by NH by the action of ammonia. This reaction generally takes place only in the presence of substances reacting with the hydrogen sulphide liberated, such as the oxides of lead or mercury. Thus, from the thio-ureas are formed the guanidines:



The thio-amides react in the same manner with ammonia in the presence of mercuric chloride.

## F. Methods for Obtaining Thio and Sulpho Compounds, and the Acid Esters of Sulphuric Acid.

**Substitution of O by S.**—The pentasulphide of phosphorus is generally employed, but in the CO group the O is also replaced by the action of hydrogen sulphide, aldehydes and ketones being thus converted into thio compounds.

Benzophenone,  $(C_6H_5)_2CO$  at  $100^\circ$ , with phosphorus pentasulphide,  $P_2S_5$ , or with an alcoholic solution of ammonium sulphhydrate, gives the mercaptan  $((C_6H_5)_2C(SH)_2$ .

Amides are converted into thio-amides by phosphorus pentasulphide; but as the reaction is very energetic, and as there may be a liberation of hydrogen sulphide and the formation of nitriles, it is better to use the anilides. Thus, formanilide,  $C_6H_5.NH.CHO$ , heated on a water-bath with  $P_2S_5$ , gives  $C_6H_5.NH.CSH$ .

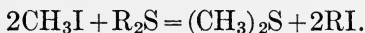
The cyanates, by the action of phosphorus pentasulphide, give sulphocyanides. The O of the OH group is replaced by S only by the use of  $P_2S_5$ . Acetic acid gives thio acetic acid.

With phenols, besides mercaptans, phosphorus pentasulphide also gives esters of phosphoric acid. For example:



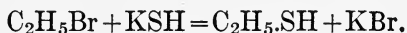
For a description of the methods of replacing O by the aid of  $P_2S_3$ , see previous pages.

**Substitution of halogens by S.**—The metallic sulphides are used for this purpose. Thus:



But the products resulting from the action of phosphorus pentachloride on anilides may be converted into thio-anilides by the action of hydrogen sulphide (thus, the compound  $C_6H_5.CCl_2.NH.C_6H_5$  is converted into thio-benzanilide).

**Substitution of halogens by HS.**—This is accomplished by heating the halogen with an aqueous or alcoholic solution of potassium sulphhydrate:



Sometimes, with mercaptans, other sulphur compounds are obtained, according to the equation:



The chlorides of the carboxyl and sulphonic acids behave in the same manner with potassium sulphhydrate. The halogen to be found in the aromatic nucleus is replaced by **HS** under the same conditions under which the **OH** group is replaced

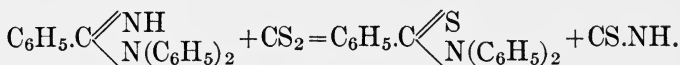
by **NH<sub>2</sub>**. Thus, nitro-dichlor-benzene,  $\text{C}_6\text{H}_3 \begin{smallmatrix} \swarrow (1) \text{Cl} \\ \searrow (2) \text{NO}_2 \\ \swarrow (4) \text{Cl} \end{smallmatrix}$ , with ammonium sulphide, gives  $\text{C}_6\text{H}_3 \begin{smallmatrix} \swarrow (1) \text{SH} \\ \searrow (2) \text{NO}_2 \\ \swarrow (4) \text{Cl} \end{smallmatrix}$ .

**Substitution of NH<sub>2</sub> by HS.**—In certain cases this can be realized by the aid of the diazo compounds. In fact, if to diazo-benzene sulphonic acid,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow \text{N} \\ \searrow \text{SO}_3 \end{smallmatrix} \text{N}$ , there is added an alcoholic solution of potassium sulphide, a liberal disengagement of nitrogen takes place, and there is formed  $\text{C}_6\text{H}_4 \begin{smallmatrix} \swarrow \text{SK} \\ \searrow \text{SO}_3\text{K} \end{smallmatrix}$ ; the reaction also gives rise to the formation of various secondary products.

**Substitution of NH by S.**—This is brought about by the direct action of hydrogen sulphide; thus,  $\text{C}_6\text{H}_5 \cdot \text{C} \begin{smallmatrix} \swarrow \text{NH} \\ \searrow \text{N}(\text{C}_6\text{H}_5)_2 \end{smallmatrix}$ , heated with hydrogen sulphide to 130° C, is converted into



The reaction takes place better on heating amidines in a sealed tube with carbon disulphide:



In the same manner the group **N.R** can also be replaced by **S**.

**Substitution of H by SO<sub>2</sub>.OH.**—This may be accomplished by the action of concentrated or fuming sulphuric acid, of the anhydride, or of chlorsulphonic acid, SO<sub>2</sub>(OH)Cl. The monosulphonic acids of the aromatic hydrocarbons are obtained by treating the latter in the cold, and more rapidly by heating with concentrated sulphuric acid. With chlorsulphonic acid, it is necessary to operate cold, or even with artificial refrigeration.

The insoluble sulphonic acids are separated by the addition of a little water; they may be recrystallized from sulphuric acid not too dilute. For the soluble acids the acid liquor is diluted with water and saturated with carbonate of lead or barium, and the salts are purified by crystallization, after having removed the insoluble sulphate by filtration. The salt is then decomposed with sulphuric acid or hydrogen sulphide. In order to separate the isomers, it is best to form the chlorides by treating with phosphorus pentachloride, and then the amides by the action of ammonia. After crystallization of the amides, the acids are set free by heating under pressure with hydrochloric acid.

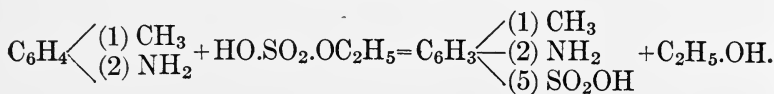
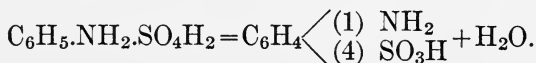
For compounds containing several sulphonic acid groups, it is better to use fuming sulphuric acid and heat, or, still better, to pass the vapors of the hydrocarbon into acid of 66° Bé. heated.

The anhydride, SO<sub>3</sub>, and chlorsulphonic acid, SO<sub>2</sub>(OH)Cl, at an elevated temperature, can give rise to sulphones; these are easily separated, owing to their insolubility in water.

The halogen and nitro substitution products of the aromatic hydrocarbons behave with sulphuric acid like the hydrocar-

bons themselves. (Bodies containing a halogen in the side-chain are carbonized with sulphuric acid.) Certain bromine and iodine compounds give with sulphuric acids certain higher halogen substitution products. Thus, dibrom-benzene,  $C_6H_4 \begin{smallmatrix} \text{Br} \\ (1) \\ \text{Br} \\ (4) \end{smallmatrix}$ , gives tetrabrom- and hexabrombenzenes.<sup>1</sup>

The amido compounds readily yield sulphonic acids on heating their sulphates, at 180–200° C, either simple or alcoholated, until water or alcohol is no longer set free.<sup>2</sup> Thus:



Both processes give good yields of the sulphonic acids.<sup>3</sup>

A particular case for obtaining the amido-sulphonic acids consists in the action of ammonium hydrosulphide on the nitro compounds.  $\alpha$ -nitro-naphthalene is converted into the ammonium salt of amido-naphthalene-sulphonic acid.

The temperature is of great importance in the production of different isomers, particularly with the phenol sulphonic acids. Chlorsulphonic acid may be employed, acting on a solution of phenol in carbon disulphide.

The carboxylic acids of the aliphatic series are converted into sulphonic acids by the anhydride,  $SO_3$ , or chlorsulphonic acid; in the aromatic series, fuming sulphuric acid is necessary, and also high temperatures.

Sulphuric acid reacts with difficulty on the pyridine nucleus. With pyridine it is necessary to heat to 320° C. Also quinoline

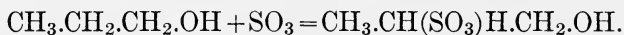
<sup>1</sup> The acid plays the part of the brominating agent. See *Berichte*, vol. 25, p. 1526.

<sup>2</sup> The action of sulphuric anhydride on the aliphatic amines is to form sulphaminic acids:  $C_2H_5.NH_2 + SO_3 = SO_2 \begin{smallmatrix} OH \\ \text{NH.C}_2H_5 \end{smallmatrix}$ .

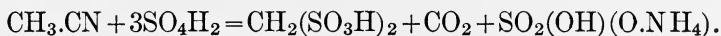
<sup>3</sup> The sulphovinic esters of the amido compounds are obtained by the double decomposition of the calcium salts with oxalates of the bases.

gives a sulphonic acid in the benzene nucleus, but not in the quinoline part of the molecule.

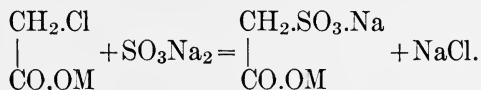
The saturated hydrocarbons and their halogen substitution products do not react with sulphuric acid. The saturated alcohols, however, react; methyl alcohol with fuming sulphuric acid gives  $\text{CH}_2(\text{OH})\text{SO}_3\text{H}$  and  $\text{CH}(\text{OH})(\text{SO}_3\text{H})_2$ . The anhydride,  $\text{SO}_3$ , gives similar bodies by uniting, not with the carbon attached to the OH (except with  $\text{CH}_3.\text{OH}$ ), but with the neighboring atom:



The amides and the nitriles, at the same time they are saponified, are also converted into sulphonic acids. Acetonitrile gives sulphacetic acid, which in its turn, under the influence of sulphuric acid, is decomposed with liberation of carbonic acid and the formation of the disulphonic acid of methane:



**Substitution of halogens by  $\text{SO}_2.\text{OH}$ .**—This is an indirect way of obtaining the sulphonic acids of the aliphatic series. This reaction takes place by the action of sulphites on halogen compounds:

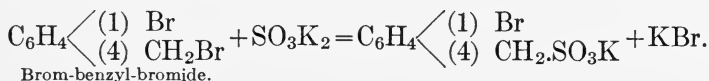


The ammonium salt may also be used. If ethyl iodide is heated with an aqueous solution of ammonium sulphite until complete dissolution, with ammonium iodide, there is formed at the same time  $\text{C}_2\text{H}_5.\text{SO}_3.\text{NH}_4$ . The mixture is diluted with water and boiled with lead oxide until ammonia ceases to be evolved; and after filtering, in order to remove the iodide of lead, there is in solution the lead salt of the sulphonic acid, which only requires to be decomposed with hydrogen sulphide.

If there is in the compound several atoms of a halogen,

these may be substituted totally or partially, according to the quantity of the salt used in the reaction. There may also be a reduction of the halogen.

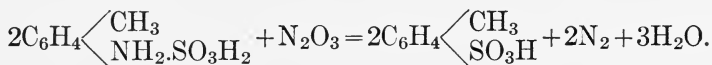
In the aromatic compounds, the halogen which is in the side-chain may also be replaced:



In derivatives of phenol, quinone, etc., it is only partially replaced. Thus, trichlor-phenol with potassium sulphite gives dichlor-phenol-sulphonate of potassium and the chlor-phenol-disulphonate.

The halogens united to nitrogen are easily replaced by sulphuric acid: the solution of the chloride,  $\text{C}_6\text{H}_4(\text{OH})\text{N}:\text{N}.\text{Cl}$  (obtained by the addition of the theoretical quantity of sodium nitrite to the cooled solution of the hydrochloride of ortho-amido-phenol), treated with potassium sulphite, gives  $\text{C}_6\text{H}_4(\text{OH})\text{N}:\text{N}.\text{SO}_3\text{K}$ .

**Substitution of  $\text{NH}_2$  by  $\text{SO}_3\text{H}$ .**—This offers an indirect means of obtaining sulphonic acid derivatives, and is effected by passing  $\text{N}_2\text{O}_3$  into a concentrated alcoholic solution of the base, saturated with sulphurous acid:



The diazo bodies behave in this manner on boiling with an alcoholic solution of sulphurous acid.

**Substitution of  $\text{OH}$  by  $\text{SO}_4\text{H}$ .**—In the aliphatic series this is accomplished as readily as the substitution of  $\text{H}$  by  $\text{SO}_3\text{H}$  in the aromatic series:

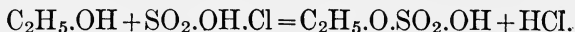


Sulphuric acid reacts so energetically with the alcohols that it is necessary to mix them with caution; the reaction is finished by heating for a time on a water-bath. On diluting



with water, the excess of sulphuric acid is removed, as already explained. The free acids are obtained very easily by means of the lead salts which are decomposed by hydrogen sulphide.

The acid esters of sulphuric acid are also obtained by adding gradually to chlor-sulphonic acid the theoretical amount of well-cooled alcohol:



The acid esters of the phenols are in general very unstable, and cannot be prepared by the action of sulphuric acid on phenols ( $\beta$ -naphthol-sulphate,  $\text{C}_{10}\text{H}_7.\text{O}.\text{SO}_2.\text{OH}$ , offers an exception, as it is formed by the direct action of sulphuric acid). In order to prepare the corresponding alkali salts, potassium pyrosulphate is added to the concentrated aqueous solution of the alkali phenate, and heated for several hours at 60–70° C. The following equation may be taken as representing the reaction:



If higher heat is used, the para-sulpho-phenol is formed.

**Substitution of H by  $\text{SO}_2\text{Cl}$ .**—This is accomplished by the action of sulphuryl chloride,  $\text{SO}_2\text{Cl}_2$ , on the alcohols and secondary amines. By gradually adding the theoretical quantity of alcohol to sulphuryl chloride and cooling, an energetic reaction takes place, hydrochloric acid being liberated, while there is formed  $\text{RO}.\text{SO}_2\text{Cl}$ , in the form of a heavy oil, which is purified by washing with cold water and drying over potash. The action of sulphuryl chloride on the hydrochloride of dimethyl-amine gives



**Substitution of  $\text{SO}_3\text{H}$  by  $\text{OH}$ .**—(See previous pages.)

### G. Methods for the Preparation of Metallo-Organic Derivatives.

The substitution of **H** by a metal occurs in the **OH** (also in **SH**), **CH<sub>2</sub>**, and **NH** groups. The hydrogen of alcoholic **OH** is replaced by the action of the alkali metals, and also (especially with the polyatomic alcohols) by the action of the oxides of barium, calcium, and lead.

In phenols the **H** of **OH** is replaced by the action of alkali metals.

In acids, the hydrogen is readily replaced by a metal by double decomposition with the salts. In order to prepare the salts of potassium, sodium, calcium, barium, and strontium, the free acid is saturated by the corresponding base. The oxides of barium, calcium, and strontium may be used in excess, and afterwards removed by saturating with carbonic acid. If the salt is not soluble in alcohol, it may be precipitated from its aqueous solution by the addition of alcohol.

The salts of potassium and sodium soluble in alcohol may be prepared by saturating the alcoholic solution of the acid with the carbonates of potassium or sodium.

The salts of the alkaline earth and heavy metals may be prepared by saturating the free acid with oxides of these metals, or by double decomposition of the alkaline or ammonium salts with barium chloride, acetate of lead, sulphate of copper, nitrate of silver, etc. This method is used for the preparation of insoluble or difficultly soluble salts. The silver salts of the aromatic acids are prepared more readily by double decomposition of the calcium salts with pure silver nitrate not containing any free acid.

The calcium, barium, and lead salts are often prepared; in order to obtain the free acid it is simply sufficient to decompose these salts with oxalic acid, sulphuric acid, or hydrogen sulphide, after having purified them by crystallization. The silver salts, not containing any water of crystallization, serve especially well for the determination of the molecular weights

of the acids; ignited at a red heat, they leave pure silver, with the exception of cuminic acid, which leaves a carbide of silver.

To prepare the acid salts, it is simply necessary to incompletely saturate the acid; one-half in the case of dibasic acids, one-third or two-thirds in the case of tribasic acids, etc.

The hydrogen of the  $\text{CH}_2$  group in carboxyl-ketonic acids is replaced by a metal not only by the action of metallic sodium, or sodium alcoholate, but even by double decomposition with salts. The copper salt of acetyl-acetic ester separates in the form of a precipitate insoluble in water when a solution of copper acetate is added to an alcoholic solution of aceto-acetic ester. The hydrogen of the  $\text{CH}_2$  of malonic ester behaves in the same manner, as is also the case with the hydrogen of the so-called nitro compounds of the aliphatic series.

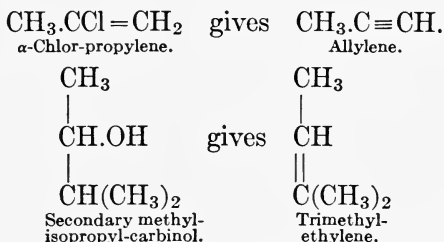
The hydrogen of the  $\text{NH}$  group of the imides may also be replaced by metals. If alcoholic sodium is added to an alcoholic solution of succinimide, followed by the addition of ether, there is precipitated  $\text{C}_4\text{H}_4\text{O}_2.\text{NK} + \frac{1}{2}\text{H}_2\text{O}$ . The silver derivative,  $\text{C}_4\text{H}_4\text{O}_2.\text{NAg}$ , is formed when silver nitrate is added to an alcoholic solution of succinimide containing a little ammonia.

When a halogen is replaced by a metal, there are formed the metallo-organic compounds. In certain cases these compounds are the result of a reaction between the intermediate products at first formed. As the metals which form such compounds are generally polyatomic, there is a condensation during the formation of the organo-metallic compounds, and an indirect complication of the molecule.

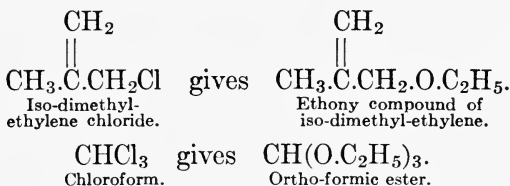
## CHAPTER IV.

### REMOVAL OF RADICALS.

**General Considerations.**—The removal of halogens and of the elements of water from organic compounds may take place when an atom of carbon, to which the halogen or **OH** is attached, is connected with one or more other atoms of carbon. The hydrogen which is removed is the one fixed to the neighboring carbon atom having the least number of hydrogen atoms.<sup>1</sup> Thus:



If there is no hydrogen fixed to the neighboring carbon atom instead of a removal of groups, there will be a substitution. Thus, with alcoholic potash:

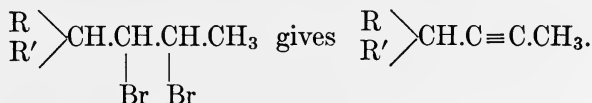
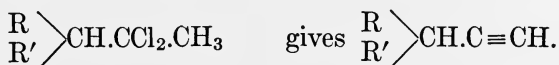
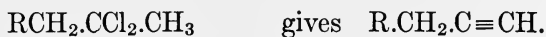



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<sup>1</sup> See V. Markovnikoff, *The Reciprocal Action of Atoms on One Another in Chemical Compounds*, Kasan, 1869 (in Russian). Also A. Zaytzeff, *On the Conditions of Fixation and Removal of the Elements of Hydriodic Acid in Organic Compounds* (*Jour. Soc. Phys. Chim. Russe*, vol. 17, p. 289).

The **alpha** isomers of the halogen substitution derivatives of the acids lose their halogen with difficulty. With alkalies they exchange the halogen for hydroxyl. Thus  $\alpha$ -chlor-propionic acid is converted completely into lactic acid, but the  $\alpha$ -brom acid is converted partly into lactic acid and partly into acrylic acid:  $\beta$ -chlor- and brom-propionic acids give only acrylic acid.

Some  $\beta$ -brom acids, heated for a long time with water, give the unsaturated acids and certain decomposition products. By removing the halogens from **gamma** derivatives, inner anhydrides, or lactones, are formed. In the aromatic series the **beta** derivatives behave in the same manner. Cold water is sometimes sufficient to bring about this reaction. When the body contains two halogen atoms, they may be removed simultaneously, the hydrogens attached to the most hydrogenated carbon atom being removed at the same time.



**Removal of Hydrogen.**—For the direct removal of this element see that of Br.

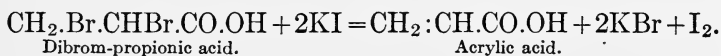
**Removal of Oxygen.**—(See previous pages.)

### A. Removal of the Halogens.

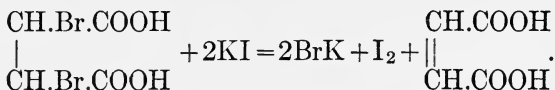
The removal of chlorine may be brought about by the action of nascent hydrogen (sodium amalgam and water, iron and acetic acid, zinc and sulphuric acid, zinc powder or copper and water), but generally it is necessary to heat the com-

pound with sodium. Sometimes the removal of chlorine is brought about by simply heating the body. Thus, by passing the vapor of hexachlor-ethane,  $\text{CCl}_3.\text{CCl}_3$ , through a heated tube, ethylene perchloride is obtained,  $\text{CCl}_2=\text{CCl}_2$ . There is also a removal of chlorine, at times, when it is endeavored to replace this halogen with iodine, especially if the atoms of chlorine are not fixed to a single carbon atom.

**The removal of bromine** is carried out more easily than that of chlorine, by the action of water, of sodium, of mercury, or with a zinc-copper element. For instance, trimethylene may be prepared by heating the bromide on a water-bath with zinc powder and dilute alcohol. In the same manner ethylene may be prepared from the bromide,  $\text{C}_2\text{H}_4\text{Br}_2$ , and the dibromide of acetylene,  $\text{C}_2\text{H}_2\text{Br}_2$ , from the tetrabromide,  $\text{C}_2\text{H}_2\text{Br}_4$ .<sup>1</sup> Bromine derivatives treated with potassium iodide also lose bromine:



In the same manner, fumaric acid may be prepared from dibrom-succinic acid:



In order to neutralize the iodine set free in the reaction, metallic copper is added to the mixture.<sup>2</sup>

**The removal of iodine**, as already indicated above, takes place sometimes in the decomposition of the iodine compounds.

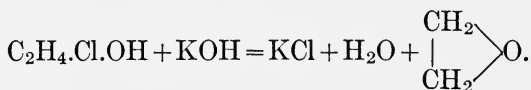
## B. Removal of the Halogen Acids.

**The removal of hydrochloric acid** is sometimes brought about by heating. Thus, the products of the action of phos-

<sup>1</sup> See A. Sabaneff, *On the Compounds of Acetylene*, Moscow, 1881 (in Russian).

<sup>2</sup> Berthelot's method.

phorus pentachloride on aldehydes, ketones, ketonic acids, amines, anilides, etc., often lose a molecule of hydrochloric acid. The second molecule is removed, as in other cases, through more or less energetic actions, as, for example, in the preparation of ethylene oxide by the action of potash on chlorhydrin:



The best method consists in using an alkaline solution, aqueous or alcoholic, and hot or cold.<sup>1</sup> Baryta-water may also be used, as well as the carbonate of silver and oxide of lead; and even recourse may be had to distillation with soda-lime. With aromatic compounds, the removal of halogen acids only takes place in cases where the halogen is in the side-chain.

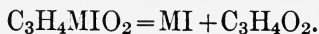
**The removal of hydrobromic acid** is more easily brought about than that of hydrochloric acid. It can be effected instantly, as when the unsaturated acids are converted into isomeric lactones, by the action of hydrobromic acid. Some methods of producing the unsaturated compounds are based on the removal of hydrobromic acid.

**The removal of hydriodic acid** is very easily effected, and very frequently the iodine compounds are used for the preparation of unsaturated derivatives.<sup>2</sup> A concentrated alcoholic solution of potash is used. This acid may also be removed by the oxides of silver or lead, and even with acetate of lead. The salts of hydriodic acid are sometimes decomposed by heating their aqueous solutions. The lead salt of iodo-pro-

<sup>1</sup> With an alcoholic alkaline solution there is usually produced, as a by-product, some ethers of RCl, as, for example, R.OC<sub>2</sub>H<sub>5</sub>.

<sup>2</sup> Occasionally through the removal of HI there are obtained two isomeric hydrocarbons. This may, perhaps, be attributed to the action of the alcoholic potash. Compare the behavior of the acetylene hydrocarbons. Iodo-stearic acid (action of HI on oleic acid), treated with alcoholic potash, loses HI and gives ordinary oleic acid, together with a solid isomer of the latter.

pionic acid,  $\text{CH}_2\text{I}.\text{CH}_2.\text{CO}.\text{OH}$ , gives acrylic acid; in a general manner this reaction may be written as:



### C. Removal of Water.

In di- and tri-hydrates, in  $\gamma$ -hydroxy acids, and some others, the removal of water takes place at the moment of their formation. But generally it occurs through the action of heat or dehydrating agents, and also through the production of intermediate compounds. Thus, the ethylene hydrocarbons are obtained by the distillation of the corresponding alcohols and ethers.

The elements of water may be removed from alcohols by heating them with fused zinc chloride, or by gradually adding them to phosphoric anhydride. The latter method is a very convenient one for the preparation of the gaseous unsaturated hydrocarbons, particularly propylene.<sup>1</sup> Water may also be removed from alcohols by passing their vapor over heated zinc powder. Concentrated (and even, in some cases, dilute) sulphuric acid also produces the same result.

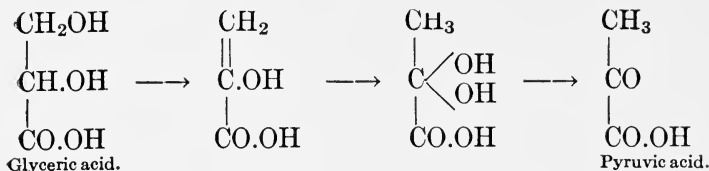
At the same time that the desired hydrocarbon is prepared, there are also formed its isomers. The removal of water is frequently accompanied by reduction.

The  $\beta$ -oxy and oxy-polycarboxylic acids behave in the same manner as the alcohols with regard to the removal of water (distillation of the free acids, action of dilute sulphuric acid and heat, phosphorus chloride, phosphoric anhydride, etc.): they are converted into the unsaturated acids. Alexeyeff admits the following series of transformations:<sup>2</sup>

<sup>1</sup> According to Beilstein.

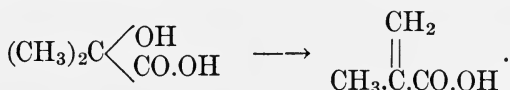
<sup>2</sup> The formation of pyruvic acid from glyceric acid is the result of several successive reactions. It is very probable that there is a removal of  $\beta$ -OH and the formation of an unsaturated oxy-acid; then, by the fixation and subsequent loss of the elements of water, the unsaturated compound is converted into pyruvic acid.





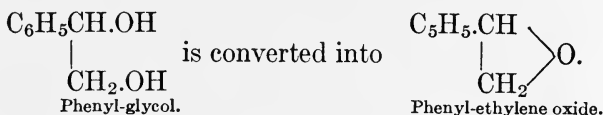
It is to be remarked that the transformation of pyruvic acid from glyceric acid is analogous to the production of aldehyde by the dehydration of glycol.

The ethers of the  $\alpha$ -acids, in which OH plays the rôle of a tertiary alcohol, are likewise comparable to the alcohols. Thus, methyl-acrylic acid is obtained by the action of phosphorus trichloride on the ether of  $\alpha$ -oxy-isobutyric acid:

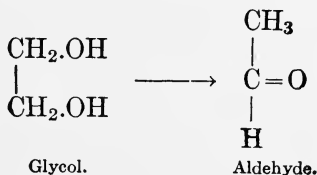


Generally, the  $\alpha$ -oxycarboxylic acids, through the loss of water (by the action of heat), give anhydrides.

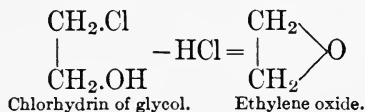
The dihydric alcohols are also converted into anhydrides (oxides) by the removal of water. This reaction is easily carried out in many cases. Thus, by boiling with dilute sulphuric acid,



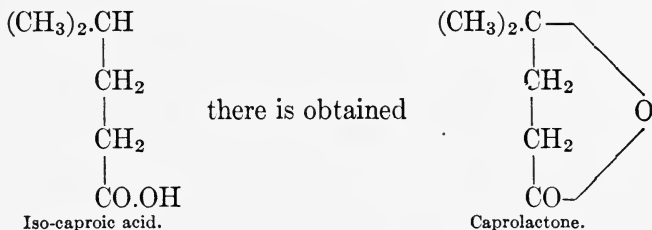
The removal of water from the ordinary glycols of the aliphatic series (by means of dehydrating agents) is accompanied by the formation of isomerides. The compounds formed are not true anhydrides but isomers, from which the glycol cannot be again regenerated by the addition of water; thus, ordinary glycol gives ethyl aldehyde:



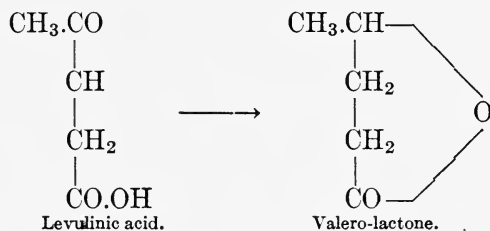
To obtain the true anhydrides it is necessary to remove the elements of hydrochloric acid from the mono-chlorhydrins:



The  $\gamma$ -hydroxy acids, as remarked above, lose water when they are formed; on this account the lactones are always formed in their place. Thus, by the oxidation of isocaproic acid,



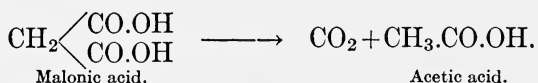
In the same manner, by the reduction of levulinic acid (a  $\gamma$ -ketonic acid), in place of obtaining the corresponding hydroxy acid, there is formed valero-lactone:



The removal of water from the aromatic hydroxy acids (OH fixed to the benzene nucleus) takes place rather difficultly; it is necessary to subject the body to dry distillation, or to the action of concentrated hydrobromic acid. In this manner it is possible to obtain coumarin from coumaric acid.

The dicarboxylic acids behave in the same manner as the

$\alpha$ -hydroxy-acids; by heating them, or by the action of dehydrating agents, they are converted into anhydrides. The acids of the aliphatic series, which have two carboxyl groups, united the one to the other (as in oxalic acid), or with one or two atoms of carbon (malonic acid and its homologues), do not give anhydrides, but are decomposed, giving rise to carbonic acid and a mono-basic acid:



In the aromatic series, the anhydrides are formed when the two carboxyl groups are in the ortho position with reference to one another, or with reference to the point which unites two benzene residues.

Simultaneously with the anhydride, there are formed, in certain cases, ketonic acids. Diphenic acid, moderately heated with concentrated sulphuric acid, gives diphenyl-ketonic acid:



Some dicarboxylic acids are converted into anhydrides by a prolonged fusion, others by repeated distillations, and some by acetic anhydride or acetyl chloride. To remove the water, sulphuric acid may be used, and also the chlorides and oxychlorides of phosphorus. When acetyl chloride is employed, it is necessary to remember that the hydroxy-dicarboxylic acids give acetyl anhydrides, and the unsaturated di-acids are converted into chlorine derivatives of the desired acid.

The ammoniacal salts of the acids, when heated, lose water and form the amides of the corresponding acids:

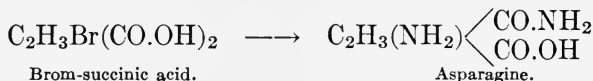


Dry distillation is sufficient, but in the majority of cases the salt is dissociated, and is decomposed into the acid and ammonia. This is particularly so with ammonium acetate  $\text{CH}_3\text{CO.ONH}_4$ , when there is only a yield of 25 per cent.; by distilling sodium acetate with ammonium chloride, the same result is obtained. Better results are obtained if the salt is heated in an autoclave for five or six hours at  $220^\circ\text{C}$ , when the yield is 80 to 85 per cent. of the theoretical. Some aromatic acids give a slightly better yield than this.<sup>1</sup>

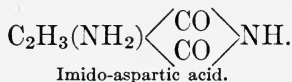
In some cases (for example, in heating the ammonium salt of isobutyric acid) a secondary amide is formed simultaneously with the primary amide.

The dicarboxylic acids, on heating, behave in the same manner: with the acid salts there are formed acid amides; with the neutral salts, amides.

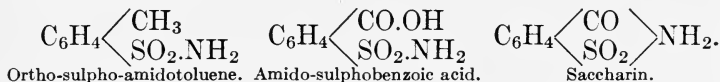
The amido acids, on losing water, are converted into imides. This reaction sometimes takes place in attempting to form the acid amides. Thus, brom-succinic ester, heated with an alcoholic solution of ammonia, gives the imide of aspartic acid, instead of asparagine:



and

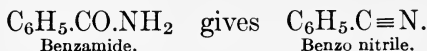


By the oxidation of ortho-sulpho-amidotoluene there is produced simultaneously amido-sulphobenzoic acid and the imide derivative, saccharin, a substance which has an exceedingly sweet taste:



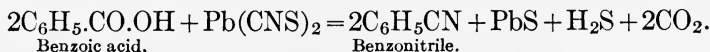
<sup>1</sup> With respect to the time and temperature of the reaction for different acids, see Menchoutkine, *Jour. Soc. Phys. Chim. Russe*, vol. 16, p. 191, and vol. 17, p. 259.

The amides, by the loss of water, are changed into nitriles:

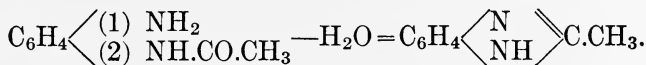


It rarely happens that water may be removed from amides by simply heating, but the intervention of a dehydrating agent is required (such as  $\text{P}_2\text{O}_5$ ,  $\text{PCl}_5$ ,  $\text{P}_2\text{S}_5$ , and  $\text{ZnCl}_2$ ).

In order to obtain nitriles, one may start with the ammonium salt of the corresponding acid and treat it with phosphoric anhydride. The aromatic nitriles are also obtained by the action of lead sulphocyanide on the acids:



The ortho-amido-anilides (1.2), on losing water, give substituted derivatives of the amidines:



The removal of water takes place at the moment of formation of ortho-amido-anilide (by the action of the chloride of the acid, or of the acid itself, on the ortho-diamido compound). Some apparent anhydrides are obtained with the derivatives of ortho-amido-phenol. Thus,  $\text{C}_6\text{H}_4 \begin{array}{c} \text{N} \\ \text{< } \text{O} \end{array} \text{> C}\cdot\text{C}_6\text{H}_5$  is prepared by the reduction of  $\text{C}_6\text{H}_4 \begin{array}{c} \text{NO}_2 \\ \text{< } \text{O}\cdot\text{CO}\cdot\text{C}_6\text{H}_5 \end{array}$ , or is produced in the action of benzoyl chloride on ortho-amido-phenol.

The aldoximes  $\text{R}\cdot\text{CH}:\text{N}\cdot\text{OH}$ , by the loss of water (with acetic anhydride), are converted into nitriles,  $\text{RC}:\text{N}$ .

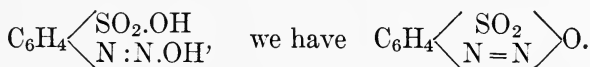
Some compounds containing nitrogen are easily decomposed with loss of water. The oxidation of choline,

$\begin{array}{c} \text{CH}_2.\text{OH} \\ | \\ \text{CH}_2.\text{N}(\text{CH}_3)_3\text{OH} \end{array}$ , instead of giving  $\begin{array}{c} \text{CO.OH} \\ | \\ \text{CH}_2\text{N}(\text{CH}_3)_3\text{OH} \end{array}$ , furnishes  
 the anhydride of betaine,  $\begin{array}{c} \text{CO-O} \\ | \quad | \\ \text{CH}_2\text{N}(\text{CH}_3)_3 \end{array}$

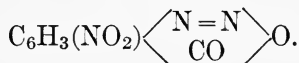
The diazo bodies of the phenols and the sulphonic acids lose water at the moment of their formation. For example, with the amido-sulphonic acid,



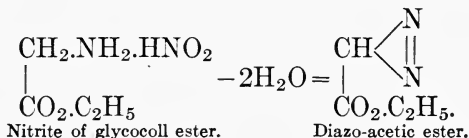
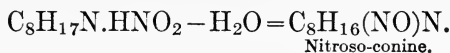
in place of obtaining



Nitro-amidobenzoic acid,  $\text{C}_6\text{H}_3(\text{NH}_2)(\text{NO}_2)\text{CO.OH}$ , in the same manner, with nitrous acid, gives:



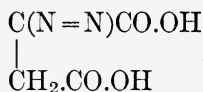
The nitrites of the secondary amines and of the esters of the amido acids of the fatty series are very unstable compounds which decompose with loss of water, and the formation of nitroso-amines and esters of the diazo-acids. Thus:



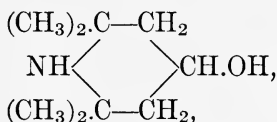
The nitrite of glycocoll may be obtained by double decomposition between the hydrochloride of the ester of glycocoll

(action of HCl in absolute alcohol on the acid amide) with silver nitrite. The ester of the diazo-acid is obtained by adding potassium nitrite to a solution of the hydrochloride of the ester of glycocoll; by the action of hydrochloric acid, there is a splitting-off of water and the formation of the diazo-compound.

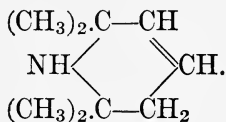
With the nitrite of aspartic ester there is obtained the ester of diazo-succinic acid:



The diazo-acids of the aliphatic series are stable only in the form of esters or amides; when liberated they decompose with loss of nitrogen. By the removal of water from the ammonium compounds of the aldehydes, there may be obtained artificially the homologues and analogues of pyridine. Acrolein-ammonia on distillation gives picoline ( $\beta$ -methylpyridine); with the ammonia derivative of crotonic aldehyde, collidine (methyl-ethyl-pyridine) is produced. The alkamine,



which is obtained by the reduction of triacetoneamine, gives, with sulphuric acid, the poisonous alkaloid triacetoneine:

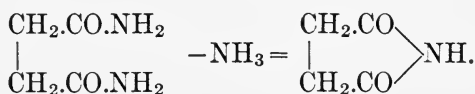


By heating normal butyric acid with pentasulphide of phosphorus, using two to three times the theoretical quantity, there is formed thiophene,  $\text{C}_4\text{H}_4\text{S}$ . Its formation can be regarded

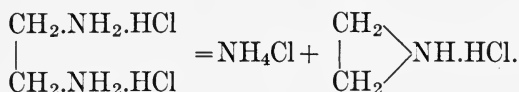
as a removal of water and hydrogen from the thio-butyric acid,  $\text{CH}_3.\text{CH}_2.\text{CH}_2.\text{CO}.\text{SH}$ , which is at first formed.

#### D. Removal of Ammonia, $\text{NH}_3$ .

When the diamines and the diamides are heated they lose  $\text{NH}_3$  and form imines and imides. Thus succinamide gives succinimide:



The hydrochloride of ethylene-diamine is decomposed, when heated, into ammonium chloride and the hydrochloride of the imine:

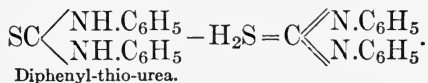
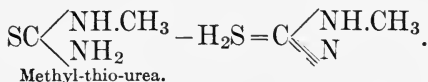


By even distilling the hydrochloride of pentamethylene-diamine (reduction of the cyanide of trimethylene) there is formed, at the same time with ammonium chloride, some of the hydrochloride of piperidine:



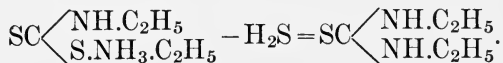
#### E. Removal of Hydrogen Sulphide.

The substituted thio-ureas lose hydrogen sulphide when treated with lead oxide, or with freshly precipitated mercury oxide. Thus:

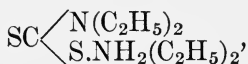




The same thio-ureas of the aliphatic series may be obtained by heating the salts of the thio-carbamic acids (obtained by the union of  $\text{CS}_2$  with  $\text{RNH}_2$ ) with alcohol in sealed tubes to  $110\text{--}120^\circ \text{C.}$ , thus causing a removal of hydrogen sulphide:

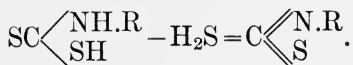


The product obtained by the combination of diethyl-amine with carbon disulphide,



is a stable enough compound in the sense that it does not lose hydrogen sulphide even when treated with metallic oxides, but it is decomposed into diethyl-amine and a salt of diethyl-thio-carbamic acid.

The substituted dithio-carbamic acids are converted into isosulphocyanic esters by loss of hydrogen sulphide:



As the acids themselves are not very stable, their lead or silver salts are used.

In order to prepare the isosulphocyanates of the aliphatic series, it is not necessary to isolate the salts of the dithio-carbamic acids; the mixture obtained by the union of the amine with carbon disulphide and the theoretical quantity of mercuric chloride may be distilled directly. The product of the union of  $2\text{R.NH}_2$  with carbon disulphide may also be treated with an alcoholic solution of iodine.

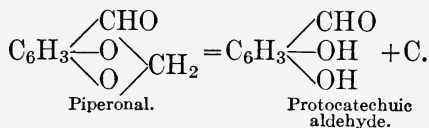
### F. Removal of Sulphuric Anhydride ( $\text{SO}_3$ ).

The removal of  $\text{SO}_3$  takes place by heating the sulphonic acids with water; with hydrochloric and hydrobromic acids to  $150\text{--}250^\circ$ , and by the dry distillation of the sulphonic

acids. This reaction is very often employed for the purification and separation of the hydrocarbons,  $C_nH_{2n-6}$ ; the best means of conducting this decomposition is with superheated steam. The dry salt of the sulphonic acid is mixed with 3 parts of sulphuric acid and 1 part of water and heated to  $180-220^\circ C.$ ; there is then passed a current of superheated steam through the mixture.

### G. Removal of Carbon (C).

This is a very rare reaction; the only example, perhaps, is the formation of protocatechuic aldehyde,  $C_7H_6O_3$ , from piperonal,  $C_8H_6O_3$ , by heating this body in a sealed tube with hydrochloric acid:



Another example of this removal would be nitrophthalide,  $C_8H_5NO_4$ , that Dussar is said to have obtained by the action of potash and calcium hydrate on nitronaphthalene,  $C_{10}H_7NO_2$ ; but in reality there may be only a removal of the impurities in the nitronaphthalene, and it is doubtful if nitrophthalide is formed.<sup>1</sup>

### H. Removal of Carbon Monoxide (CO).

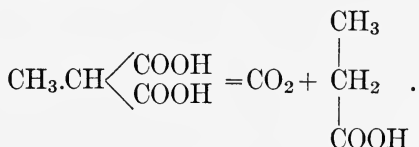
The aldehydes and ketones, on energetic heating, lose CO. Thus benzoic aldehyde,  $C_6H_5.CHO$ , gives benzene,  $C_6H_6$ ; benzophenone,  $C_6H_5.CO.C_6H_5$ , and acetophenone,  $C_6H_5CO.CH_3$ , are transformed, the first into diphenyl,  $C_6H_5.C_6H_5$ , the second into toluene,  $C_6H_5.CH_3$ . This reaction is not very complete as there is formed a large amount of other products.

<sup>1</sup> See Fehling's *Handwörterbuch*, Bd. V, p. 508, and *Jour. Soc. Phys. Chim. Russe*, vol. 2, p. 266. See also *Annalen*, vol. 202, p. 219.

### I. Removal of Carbonic Acid (CO<sub>2</sub>).

The monocarboxylic acids of the formula R.COOH, by losing CO<sub>2</sub>, give the hydrocarbons, RH; it is only necessary to heat them with the hydrates or oxides of calcium or barium.

The dicarboxylic acids of the aliphatic series lose CO<sub>2</sub> much more easily, and are converted into a monocarboxylic acid when the two COOH groups are attached to a single carbon atom. Such are malonic acid and its substituted derivatives. Thus, methyl-malonic acid (iso-succinic) is split up into carbonic and propionic acids:

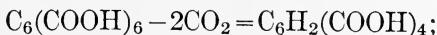


It is only necessary to fuse the acid and heat it to 180–220° C.

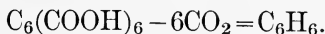
Some tricarboxylic acids are also decomposed easily; for example, aconitic acid. Desoxalic acid heated in aqueous solution is decomposed into CO<sub>2</sub> and para-tartaric acid.

Acids which yield anhydrides (oxalic, succinic) lose CO<sub>2</sub> under the influence of uranium salts (particularly the nitrate) when exposed to sunlight. To remove CO<sub>2</sub> from aromatic dibasic acids, they are heated with lime.

It is possible to remove more than one CO<sub>2</sub> group from polycarboxylic acids. Thus mellitic acid, on dry distillation, gives pyromellitic acid,



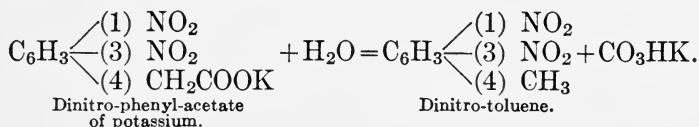
and, by heating with soda-lime, benzene is produced:



Mellitic acid above 200° C. loses 2CO<sub>2</sub>; fused with soda, it gives benzene and carbonic acid.

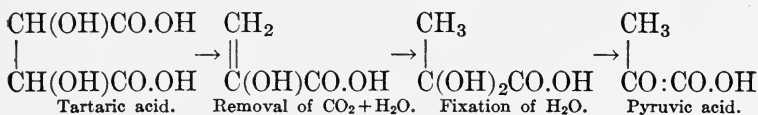
To remove  $\text{CO}_2$  from chlorinated products of the aromatic acids they are heated in a sealed tube with dilute sulphuric acid; distillation with lime would remove the halogen.

The nitro-carboxylic acids lose  $\text{CO}_2$  less easily. However, the alkaline dinitro-phenyl-acetates are decomposed slowly at the ordinary temperature, and instantly on boiling with water:



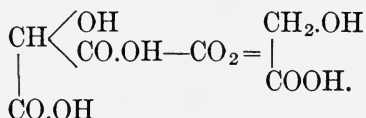
The amino-acids are easily converted into amines by heating alone, or with soda-lime; with caustic potash or with baryta-water in sealed tubes. Glycocoll gives methylamine, and the amino-benzoic acids give aniline.

The aliphatic hydroxy-acids lose  $\text{CO}_2$  with difficulty; for if they are heated, in the majority of cases, they are decomposed, with loss of water or formic acid. Sometimes the removal of  $\text{CO}_2$  is accompanied by the loss of water. This occurs, for instance, in the preparation of pyruvic acid, starting from tartaric acid, although, in fact, this reaction may be more complicated, the formation of pyruvic acid taking place through the intervention of unsaturated compounds:



It may be admitted that tartaric acid at first loses  $\text{CO}_2$  and gives glyceric acid, which then will give pyruvic acid.

Tartronic acid, by the loss of water, gives glycollic acid (in fact, its anhydride):



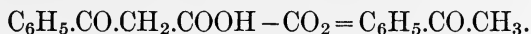
The aromatic hydroxyl acids readily lose  $\text{CO}_2$  on distillation, alone or mixed with pumice-stone, lime, or baryta. Gallic acid heated with water in a closed vessel to  $200\text{--}210^\circ\text{C}$ . gives pyrogallol through loss of  $\text{CO}_2$ ; with phloroglucic acid,  $\text{C}_6\text{H}_2(\text{OH})_3\text{COOH}$ , the decomposition takes place more readily, the latter being converted completely into phloroglucinol by simply boiling with water.

Pyridine- and quinoline-carboxylic acids, on distillation with lime, are decomposed with loss of  $\text{CO}_2$ . Thus, nicotinic acid ( $\beta$ -pyridine-carboxylic acid) gives pyridine. The pyridine-dicarboxylic acids, when heated alone, give pyridine-carboxylic acids; the  $\alpha$ - $\beta$ -dicarboxylic acid gives nicotinic acid:

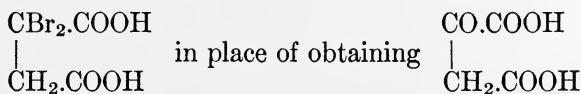


If it is distilled with lime, two  $\text{CO}_2$  groups are removed.

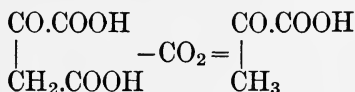
Ketonic acids, such as aceto-acetic acid and others in which the CO and COOH groups attached to one and the same carbon atom, lose  $\text{CO}_2$  with especial ease (some above  $100^\circ\text{C}$ .), and are converted into ketones:



Sometimes the splitting off of  $\text{CO}_2$  takes place at the moment of formation of a compound. Thus, in treating an aqueous solution of the salt of iso-dibrom-succinic acid with silver oxide,



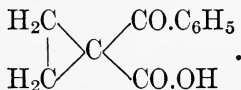
there is obtained the decomposition product, pyruvic acid and  $\text{CO}_2$ :



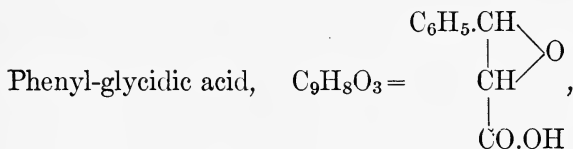
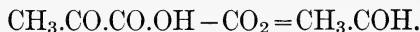
In order to obtain ketones from the ketonic acids, they are decomposed with a dilute solution of caustic potash.

In certain cases it is preferable to heat the ester with dilute sulphuric and hydrochloric acids, or with water alone. The esters of the diketonic acids may be used in the same manner (the diketones are easily decomposed with alkalies), as well as the halogen substitution products of the ketonic acids.

There are some ketonic acids containing CO and COOH groups attached to a single carbon atom, which are, however, more stable; these are not decomposed by saponification of their esters; they lose CO<sub>2</sub> only after energetic heating; for example, the body



Pyruvic acid, heated with dilute sulphuric acid, loses CO<sub>2</sub> and gives the aldehyde:



at the ordinary temperature, is decomposed with liberation of CO<sub>2</sub>.

#### J. Removal of Formic Acid (HCO.OH).

Hydrophthalic acid, C<sub>8</sub>H<sub>8</sub>O<sub>4</sub>, with sulphuric acid, gives phthalic acid, at the same time with benzoic acid, carbon monoxide, and water:

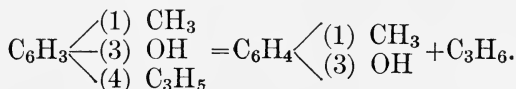


**K. Removal of Acetic Acid ( $\text{CH}_3\text{CO.OH}$ ).**

(See Chapters VII and VIII.)

**L. Removal of a Hydrocarbon.**

This reaction occurs in the decomposition of the esters of the alcohols. The action of phosphoric anhydride on phenols also takes place in the same manner. Thymol, for example, is decomposed into propylene and meta-cresol:

**M. Removal of Alcohol ( $\text{R.OH}$ ).**

In a body which readily loses water, if the hydrogen of the OH group is replaced by a radical R, for example,  $\text{C}_2\text{H}_5$ , it is almost certain that the compound will be decomposed with loss of alcohol. The hydrates of substituted ammonias behave in the same manner; on heating them, they are decomposed into a compound in which the nitrogen is triatomic, and into an alcohol, or the products of its decomposition, hydrocarbon and water.

**N. Removal of Simple Ethers.**

The halogen products of the ammonium compounds, like  $\text{R}_4\text{NI}$ , are decomposed by strong heat into  $\text{NR}_3$  and  $\text{IR}$ . If the four radicals are not identical, and if they include a  $\text{CH}_3$  group, the latter will combine with the halogen.

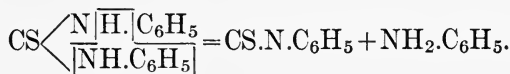
**O. Removal of Amines ( $\text{NH}_2\text{R}$ ).**

The symmetrical urea compounds are decomposed by the action of acids into isocyanic esters and amines:

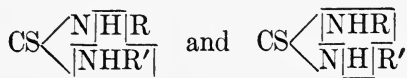


The thio-ureas behave in the same manner, and this reaction is utilized for the preparation of iso-sulphocyanides of the aromatic series; the reaction also takes place in the aliphatic series, but it is not made use of.

In the aromatic series, the thio-ureas are heated with sulphuric or hydrochloric acid; it is better, however, to use a concentrated solution of phosphoric acid (sp. gr.=1.7), two or three parts of this solution to one part of the thio-urea. After heating for a short time, the iso-sulphocyanate is volatilized with steam, and in the residue the amine is removed with an alkali. Diphenyl-thio-urea is thus completely decomposed:



When the thio-ureas contain two different radicals, there are obtained two sulphocyanides and two amines, the decomposition being effected in two directions:





## CHAPTER V.

### DIRECT FIXATION OF GROUPS.

#### I. GENERAL CONSIDERATIONS.

In the direct fixation of halogen acids<sup>1</sup> to unsaturated hydrocarbons, the halogen attaches itself to the carbon atom having the least amount of hydrogen.<sup>2</sup> In cases where two atoms of carbon may be equal in this respect, the halogen combines with that one to which a methyl group (CH<sub>3</sub>) is attached:

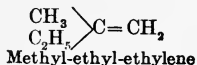


<sup>1</sup> See Markovnikoff and A. Zaytzeff as referred to on p. 108. See also Kablukoff, *On the Triatomic Alcohols and their Derivatives*, Moscow, 1887 (in Russian).

<sup>2</sup> Among the unsaturated hydrocarbons, those containing a carbon atom attached to the least number of hydrogen atoms combine the most readily with the halogen acids. This property may be used for the separation of isomers. Thus, the two isomeric amylenes



and



cannot be satisfactorily separated by distillation, as the former boils at 21° C. and the latter at 32° C. At 20° C., however, the latter alone gives the iodo-compound:

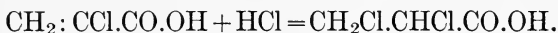
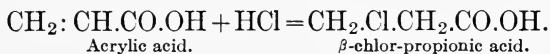


and this boils at above 100° C.

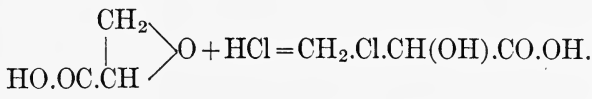
With hydrocarbons having the group  $-C\equiv C-$ , two atoms of the halogen are fixed to the carbon atom with the least hydrogen.



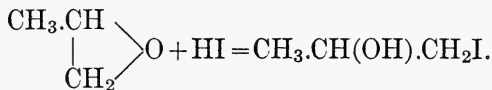
Aldehydes and unsaturated acids, by the fixation of a halogen acid, most often form the  $\beta$ -substituted body of the saturated compound:



With oxides containing the  $\begin{array}{c} C \\ | \quad \diagup \\ C \quad O \end{array}$  group, the halogen attaches itself to the carbon atom with the most hydrogen, and the OH group, which is formed, to the carbon atom with the least hydrogen:



It is possible to obtain in this manner the iodo substitution products of the alcohols:



In the fixation of the halogen acids to the unsaturated alcohols, there is a displacement of OH by halogen (see page 79).

With hydrobromic acid, there are often two isomers formed; by modifying the conditions it is possible to direct at will the reaction in one way or the other. In the majority of cases the reaction proceeds normally (the bromine being fixed by the carbon atom with the least hydrogen) if the hydrobromic acid is not very concentrated. Thus, brom-ethylene, with acid satu-

rated at  $6^{\circ}\text{C}$ ., gives mostly ethylene bromide,  $\text{CH}_2\text{Br}.\text{CH}_2\text{Br}$ ; but if the acid is diluted with two volumes of water, ethylidene bromide is formed,  $\text{CH}_3.\text{CH}.\text{Br}_2$ . The temperature of the reaction also exerts an influence: thus, atropic acid ( $\alpha$ -phenyl-acrylic),  $\text{CH}_2=\text{C}(\text{C}_6\text{H}_5).\text{CO}.\text{OH}$ , at  $100^{\circ}\text{C}$ ., with concentrated hydrobromic acid, gives  $\beta$ -brom-hydratropic acid; but at the ordinary temperature, a mixture of the  $\alpha$ - and  $\beta$ -acids is obtained.

The carbon atom to which the halogen attaches itself, in the case of the fixation of a halogen acid, is the same one as that to which the OH group attaches itself in the case of the fixation of water.

## II. FIXATION OF HYDROGEN (H).

(See under Chapter II.)

## III. FIXATION OF OXYGEN (O).

To the reactions already mentioned in Chapter I, there will be added here the case of the fixation of oxygen to compounds containing sulphur, nitrogen, or metals.

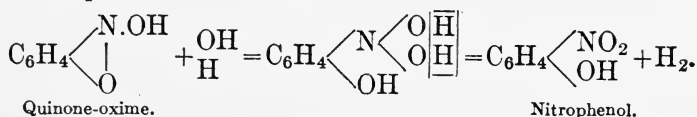
The sodium mercaptan,  $\text{C}_2\text{H}_5.\text{SNa}$ , with dry oxygen, combines with  $\text{O}_2$  and is converted into  $\text{C}_2\text{H}_5.\text{SO}_2\text{Na}$ . The same mercaptan, as well as other bodies of the type  $\text{R}.\text{SH}$ , are oxidized by nitric acid, and by the fixation of  $\text{O}_3$  give the acids  $\text{R}.\text{SO}_2\text{OH}$ . The sulphur compounds  $\text{R}_2\text{S}$  are oxidized equally by nitric acid or potassium permanganate; by regulating the concentration and temperature, it is possible to fix O or  $\text{O}_2$  and to obtain the oxides  $\text{SOR}_2$  or the sulphones  $\text{SO}_2\text{R}_2$ .<sup>1</sup>

Iso-propyl-pseudonitrol,  $(\text{CH}_3)_2\text{C}(\text{NO})\text{NO}_2$  (see page 83), oxidized with chromic acid, is converted into dinitro-isopropane,  $(\text{CH}_3)_2.\text{C}(\text{NO}_2)_2$  (?); but it is not possible to affirm that there is here a conversion of the NO group into  $\text{NO}_2$ . It may be that there are several successive reactions, as, for example, in the

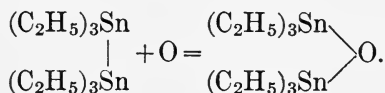
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<sup>1</sup> See A. Zaytzeff, *Action of Nitric Acid on some Organic Compounds containing Sulphur*, Kasan, 1868 (in Russian).

transformation of quinone-oxime (nitrosophenol, see page 83) into nitrophenol:



Many metallo-organic compounds readily combine with oxygen and form oxides:



When zinc-ethyl is slowly oxidized in ethereal solution, there is formed  $\text{Zn}(\text{C}_2\text{H}_5)_2\text{O}$ , and finally zinc ethylate  $(\text{C}_2\text{H}_5\text{O})_2\text{Zn}$ .

#### IV. FIXATION OF HALOGENS.

##### A. The Fixation of Chlorine (Cl).

This takes place directly with unsaturated compounds, such as ethylene. Chlorine or the trichloride of antimony is used, or the body is slightly heated with a mixture liberating chlorine ( $\text{MnO}_2$  with  $\text{NaCl}$  and  $\text{H}_2\text{SO}_4$ ). Sometimes with chlorine there are formed substitution products; this reaction is indicated by the evolution of hydrochloric acid gas.

It is necessary to take into account the part played by light in the action of chlorine. Thus,  $\alpha$ -propylene chloride,  $\text{CH}_3.\text{CCl}=\text{CH}_2$ , in the dark gives substitution products; in the light, an addition product. The unsaturated compounds, when brominated or iodinated, likewise fix chlorine, the latter with replacement of iodine by chlorine. For example, allyl iodide,  $\text{CH}_2=\text{CH}.\text{CH}_2\text{I}$ , with chlorine, gives the trichlorhydrin of glycerol:



Phenyl iodide does not lose iodine, but gives an addition product,  $\text{C}_6\text{H}_5\text{I}.\text{Cl}_2$ , by the action of chlorine on its solution in chloroform.

In order to fix chlorine to alcohols, ethers, etc., which are

unsaturated, the method of procedure is to pass a current of chlorine gas into their solution in carbon disulphide.

### B. Fixation of Bromine (Br).

In order to fix bromine to unsaturated gaseous hydrocarbons, they are passed into liquid bromine, covered with a layer of water, until the bromine is decolorized. The reaction may also be carried out by using a large vessel filled with the gas and provided with a reservoir of bromine. The bromine is added drop by drop, and the flask is shaken well; the gas may be led in continually from a gasometer. This method of operation is a good one for the fixation of bromine by ethylene.

For liquid substances bromine water may be used, or the bromine itself may be added directly to the well-cooled substance, if necessary diluting with carbon disulphide, chloroform, ether, or glacial acetic acid; the bromine being added drop by drop until the red color of an excess of bromine is noticeable. With solid bodies it is best to shake their solutions in one of the above-named solvents with bromine.<sup>1</sup> If an excess of bromine is undesirable, a quantity of bromine slightly less than the theoretical is taken. In order to avoid a violent reaction, the substance is placed under a watch-glass with a vessel containing the theoretical amount of bromine, so arranged that the compound is brominated by the absorption of the bromine vapors. If the substance is easily oxidized, it is necessary to dry it carefully. There sometimes arise secondary reactions: iodine compounds not only fix bromine, but also exchange their iodine for bromine; and the unsaturated acids, in fixing bromine with liberation of hydrobromic acid, may give brominated lactones.

Compounds having the  $C \equiv C$  group can take up  $Br_2$  and  $Br_4$ ; the first with ease, and the latter with more difficulty.

Para-nitrophenyl-propionic acid,  $C_6H_4 \begin{matrix} \swarrow (1) NO_2 \\ \searrow (4) C \equiv C.CO.OH \end{matrix}$ , only

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<sup>1</sup> See A. Verigo, *Direct Fixation in the Azo-benzene Group*, Odessa, 1871 (in Russian).

takes up  $\text{Br}_2$ . The reaction may be so energetic that there is sometimes a decomposition of the body, and, even by the regulated action of bromine in theoretical amount, it is impossible to avoid the formation of some tetrabromide.

### C. Fixation of Iodine (I).

This takes place with more difficulty than that of chlorine or bromine. Compounds containing  $\text{C}\equiv\text{C}$  only take up  $\text{I}_2$ , and even that with but little energy. For example, to combine toluene



with iodine, it is necessary to heat their mixture to fusion. In order to fix iodine, either the gaseous body is passed over iodine, or the substance is treated with the latter dissolved in carbon disulphide, chloroform, or potassium iodide. The iodides of the ammonium compounds combine readily with iodine. Thus,  $\text{NR}_4\text{I} \cdot \text{I}_2$  and  $\text{NR}_4\text{I} \cdot \text{I}_4$  are formed by adding an alcoholic solution of iodine to a solution of  $\text{NR}_4\text{I}$ .

## V. FIXATION OF HALOGEN ACIDS.

Hydrobromic acid is fixed with more difficulty than hydriodic acid, but less readily than hydrochloric acid. The action of hydrochloric or hydrobromic acid takes place either at the ordinary temperature or by heating in sealed tubes. In place of the aqueous solutions of the acids, their solutions in glacial acetic acid may at times be used.

When using hydrobromic acid, it must not be forgotten that there may also be a splitting-off of  $\text{HBr}$ ; and, if the combination contains chlorine, this may be replaced by bromine.

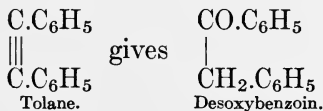
Concentrated hydriodic acid acts either cold or hot, either at the ordinary pressure or in sealed tubes. It must be borne in mind that this acid also acts as a reducing agent. Thus, allyl iodide,  $\text{C}_3\text{H}_5\text{I}$ , with hydriodic acid, gives  $\text{C}_3\text{H}_6\text{I}_2$ , which is partially reduced to isopropyl iodide,  $(\text{CH}_3)_2\text{CHI}$ , and partially

decomposed into propylene,  $\text{CH}_3\text{CH=CH}_2$  and  $\text{I}_2$ . In order to treat volatile liquids with hydriodic acid, Lagermark proceeds as follows: In a tube is placed some phosphorus iodide, a glass capsule containing the theoretical quantity of water, and a small tube containing the substance; the tube is sealed and placed in a refrigerating mixture, the capsule is broken, and when the tube is removed from the cooling mixture the reaction is finished.

## VI. FIXATION OF WATER.

The fixation of water to hydrocarbons of the ethylene and acetylene series takes place through the agency of sulphuric acid. At first there is formed an addition product with sulphuric acid ( $\text{H}$  and  $\text{O.SO}_2\text{OH}$ , which add themselves like  $\text{H}$  and halogens in the case of halogen acids), which is decomposed by water into an alcohol in the case of ethylene derivatives, and into an aldehyde or a ketone (anhydrides of dihydrates) in the case of acetylene compounds. The hydrocarbon is easily and quickly absorbed by the sulphuric acid (2 to 3 parts of acid to 1 part of water). It is necessary to cool the mixture well, otherwise there may be a polymerization.

Sulphuric acid also allows of the fixing of water to compounds containing double or triple bonds between carbon atoms:



The unsaturated acids of the acrylic series are converted into oxy-acids.

Oleic acid,  $\text{C}_{18}\text{H}_{34}\text{O}_2$ , gives oxy-stearic acid,  $\text{C}_{18}\text{H}_{35}(\text{OH})\text{O}_2$ . When there should be obtained  $\gamma$ -oxy-acids by the action of sulphuric acid on unsaturated acids, lactones are formed instead.

The salts of mercury permit of the convenient addition of water to the derivatives of acetylene (method of Koutcheroff).<sup>1</sup>

<sup>1</sup> *Jour. Soc. Phys. Chim. Russe*, vol. 15, p. 575.

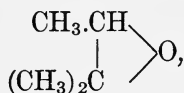
Dilute nitric acid furnishes a means of adding water to the unsaturated compounds. It is in this manner that isobutylene is converted into tertiary butyl alcohol; croton aldehyde, among other products, gives aldol. There may also be obtained the hydrate of terpene by this method.

The elements of water may also be fixed directly; fumaric acid, heated with water to 150–180° C., gives malic acid.

The oxides and anhydrides of acids containing the group  $\begin{array}{c} \text{C} \\ \diagup \\ \text{C} \end{array} \text{O}$  add the elements of water by boiling their aqueous solutions, or simply by exposure to the air at ordinary temperatures.

The ease with which the elements of water are affixed decreases with increase in the molecular weight.

Oxides containing a tertiary radical, such as

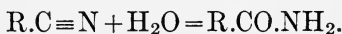


readily affix water even in the cold.<sup>1</sup> For hydrolysis accompanied by reduction, see under Chapter II.

The anhydrides of polycarboxylic acids are converted into acids, some by the action of water, and others only by the action of alkalies or alkaline carbonates; some of these acids, when their salts are decomposed, are converted into anhydrides and water.

Coumarin affixes water through the medium of alkalies, and gives an acid isomeric with coumaric acid, existing only, however, in the form of a salt; alkalies convert these salts into the corresponding salts of coumaric acid.

Nitriles, by affixing water, are converted into amides.



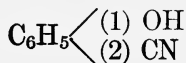
In neutral liquids, the fixation of water takes place slowly and incompletely; to increase the speed of the reaction it is necessary to use an alkaline or an acid medium. It is generally

<sup>1</sup> *Jour. Soc. Phys. Chim. Russe*, vol. 14, p. 355; and Prjibuitek, *On the Organic Dioxides*, St. Petersburg, 1887 (in Russian).



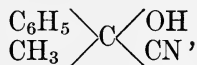
customary to use an excess of dilute hydrochloric or sulphuric acid, and to heat, if necessary, in a sealed tube.

It must be borne in mind that with an energetic reaction, as with acids or alkalies, the amide in its turn is partially, and sometimes entirely, converted into the acid. Often, even for the preparation of carboxylic acids, in place of the amide, the nitrile may be used directly. Some nitriles, especially in the aromatic series, are very unstable. Thus,



is converted into salicylic acid simply by prolonged fusion with alkalies; the nitrile,  $\text{C}_6(\text{CH}_3)_5\text{CN}$ , is not converted into the acid.

The nitriles may be saponified by means of hydriodic acid, but reduction often takes place. One of the best means of obtaining hydro-atropic acid consists in saponifying the product of the action of HCN on acetophenone:



which, on saponification, changes OH into H and gives



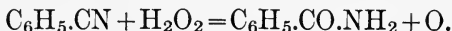
In order to convert the nitriles  $\text{R} \cdot \text{CO} \cdot \text{CN}$  into amides without forming acids, they are treated in the cold with the theoretical amount of fuming hydrochloric acid.

Cyanogen in aqueous solution is converted almost entirely into oxamide by the addition of a small quantity of aldehyde. This reaction may be explained by the successive formation and destruction of a dihydrate.<sup>1</sup>

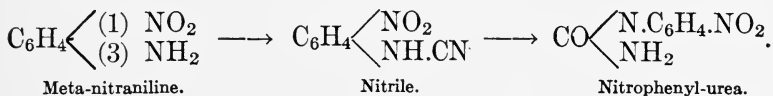
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<sup>1</sup> It is interesting to recall that this fact was discovered by Liebig while searching for a synthesis of malic acid by means of aldehyde and nascent oxalic acid (see J. Liebig's and Wöhler's *Briefwechsel*, Bd. II, p. 78).

Hydrogen peroxide also converts nitriles completely into amides with liberation of oxygen. Thus:

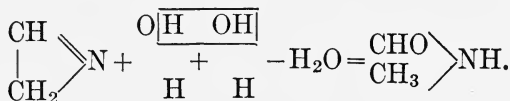


Some nitriles affix the elements of water with particular ease. If moist cyanogen chloride is passed through an ethereal solution of meta-nitraniline, there is at first formed a nitrile which subsequently affixes water and is converted into nitrophenylurea:



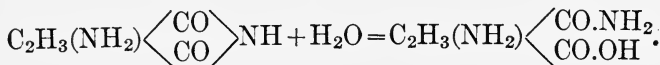
The amides,  $\text{R}.\text{CO}.\text{NH}_2$ , by the fixation of water, give the ammonium salts,  $\text{R}.\text{CO}.\text{ONH}_4$ . This reaction has been considered as a replacement of  $\text{NH}_2$  by  $\text{OH}$  (Chapter I).

The iso-nitriles by the fixation of water are converted into substituted derivatives of formamide:



Some iso-nitriles absorb water with so much energy that they convert glacial acetic acid into acetic anhydride.

The imides, by the fixation of water, give acid amides; it is sufficient to heat them with baryta-water or lime-water, and in some cases with ammonia. The imide of aspartic acid (see page 116) gives asparagine:

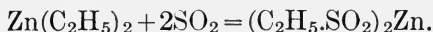


**The Fixation of Hydrogen Peroxide ( $\text{HO}.\text{OH}$ ).**—This occurs with ethylene and gives ethylene glycol. Oxidation accom-

panied by hydration is another thing than the fixation of the elements of hydrogen peroxide (see chapter on Oxidation).

**The Fixation of Hydrogen Sulphide ( $\text{H}_2\text{S}$ ).**—This occurs with nitriles in the formation of thio-amides. The nitrile in alcoholic solution is treated with ammonium sulphhydrate at the ordinary temperature, or by heating in sealed tubes.

**The Fixation of Sulphurous Anhydride ( $\text{SO}_2$ ).**—This occurs, for example, with zinc-ethyl:



For the preparation of the sodium salt of sulphinic acid, see under Chapter I. Benzene sulphinic acid,  $\text{C}_6\text{H}_5.\text{SO}.\text{OH}$ , occurs as the result of the addition of  $\text{SO}_2$  to  $\text{C}_6\text{H}_5$  in the presence of aluminium chloride.

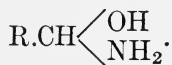
**The Fixation of Bisulphites ( $\text{MHSO}_3$ ).**—This occurs readily with aldehydes, the oxide of ethylene and its analogues.

**The Fixation of Sulphuric Anhydride** (see page 103).

**The Fixation of Sulphuric Acid** (see page 135).

## VII. FIXATION OF AMMONIA ( $\text{NH}_3$ ).

Many aldehydes combine with ammonia to form hydroxy-amines:



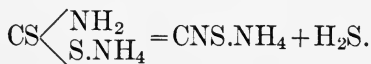
The method of carrying out this reaction is to pass a current of ammonia gas through a cooled solution of the aldehyde in ether or chloroform, or to add to the aldehyde an alcoholic or aqueous solution of ammonia.

In the same manner, the unsaturated acids can unite with ammonia; crotonic acid,  $\text{C}_4\text{H}_6\text{O}_2$ , heated in a sealed tube ( $100$ – $115^\circ \text{C}$ .), with an aqueous solution of ammonia, forms  $\beta$ -amido-butyric acid,  $\text{C}_4\text{H}_7(\text{NH}_2)\text{O}_2$ .

Carbonic anhydride combines with two molecules of ammonia, giving the ammonium salt of carbamic acid:

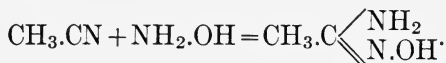


Carbon disulphide, heated with ammonia in aqueous or alcoholic solution, forms some sulphocyanide and some sulphhydrate of ammonium, but these products may be considered as coming from the decomposition of the ammonium thiocarbamate which is at first formed:



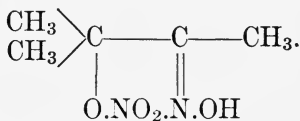
The iso-cyanic esters and the iso-sulphocyanides combine with ammonia to give substituted derivatives of urea and thio-urea.

The nitriles combine with ammonia to give amidines. For substituted derivatives of the amidines, see previous pages. The combination of hydroxylamine with nitriles gives amido-oximes or oximes:



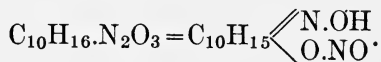
## VIII. FIXATION OF OXIDES OF NITROGEN AND NITROSYL CHLORIDE.<sup>1</sup>

By passing nitrous anhydride (arsenious acid and concentrated nitric acid) into a cooled acetic solution of amylene, the body  $\text{C}_5\text{H}_{10}.\text{N}_2\text{O}_4$  is formed. This is considered as a derivative of trimethyl-ethylene, and without doubt has the formula:



<sup>1</sup> See Wallach, *Annalen*, vols. 239, 241, 245, and 248; also N. Bunge, *On Nitroso Derivatives*, Kieff, 1868 (in Russian); and *Jour. Soc. Phys. Chim. Russe*, vol. 1, p. 257.

With a nitrite and acetic acid it is possible to affix  $\text{N}_2\text{O}_3$ . Terpene yields a crystalline body (nitrosite?):



Nitrosyl chloride combines in the same manner with terpene to give  $\text{C}_{10}\text{H}_{15} \begin{array}{l} \diagup \text{N.OH} \\ \diagdown \text{Cl} \end{array}$ , when it is passed into a solution of terpene in chloroform cooled to  $10^\circ \text{C}$ ., or when concentrated hydrochloric acid is allowed to act on a cooled mixture of terpene and nitrous ether. All these compounds are characterized by the ease with which the groups,  $\text{O.NO}_2$  and  $\text{O.NO}$ , as well as  $\text{Cl}$ , are replaced by ammonia, amines, potassium cyanide, etc.

### IX. FIXATION OF HYPOCHLOROUS ACID ( $\text{Cl.OH}$ ).<sup>1</sup>

Hypochlorous acid, in reacting with unsaturated compounds, gives nearly always two iso-merides. With acrylic acid,  $\text{CH}_2=\text{CH.CO.OH}$ , for instance, it gives:



Often the  $\text{OH}$  of hypochlorous acid is attached to the same carbon atom as the  $\text{Cl}$  when reaction with this acid occurs.

The reaction with hypochlorous acid is carried out in the following manner: Freshly precipitated oxide of mercury is mixed with water, and chlorine is passed into the mixture during constant stirring; then a fresh quantity of mercury oxide is added. This solution of hypochlorous acid may be used directly, or it is distilled in a strong current of carbon dioxide gas in

<sup>1</sup> See P. Melikoff, *On Derivatives of the Isomeric Crotonic Acids*, Odessa, 1885 (in Russian); and *Jour. Soc. Phys. Chim. Russe*, vol. 19, p. 524; also C. Reformatsky, *Polyatomic Alcohols*, Kasan, 1889 (in Russian).

order to carry off the chlorine. When the reaction is finished the excess of hypochlorous acid is removed by the addition of sodium hyposulphite. Hypochlorous acid may be replaced by calcium hypochlorite to which boric acid is added.

The fixation of hypochlorous acid is employed especially for the preparation of chlorhydrins of the polyhydric alcohols.

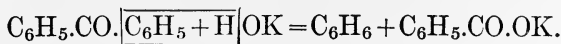
## CHAPTER VI.

### FIXATIONS ACCOMPANIED BY A DECOMPOSITION OF THE MOLECULE.

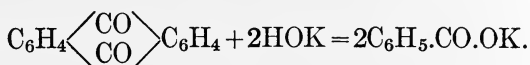
#### I. FIXATION OF WATER (HYDRATION).

##### A. Hydration followed by a Rupture of Carbon Bonds.

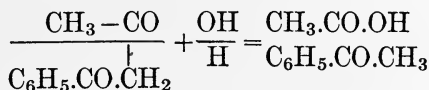
MANY of the aromatic ketones, fused with potash or distilled with soda-lime, are decomposed into hydrocarbons and salts of the acids:



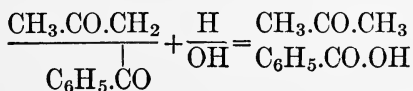
It is necessary at times to employ boiling alcoholic potash. Anthraquinone is converted into benzoic acid by fusion with potash at 250° C.:



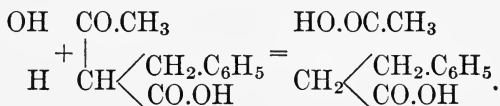
Diketones (see page 126) are readily decomposed with the addition of water by boiling with alkalies or acids, and yield ketones and carboxylic acids:



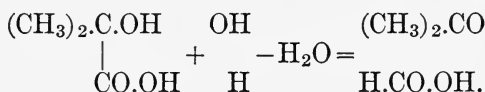
A certain quantity of the diketone is also decomposed at the other keto group, yielding the corresponding acid and ketone:



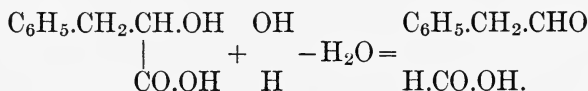
The ketonic acids, like aceto-acetic acid and its derivatives, with concentrated solutions of the alkalies, are decomposed with the formation of carboxylic acids. Thus, aceto-acetic acid, or its ester (which is saponified during the reaction), yields two molecules of acetic acid; and benzyl-aceto-acetic acid (or its ester) gives benzyl-acetic acid (hydrocinnamic acid) and acetic acid:



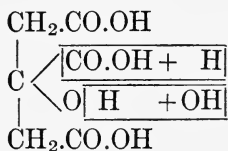
In the same manner, by heating carboxylic and hydroxy-acids with dilute sulphuric acid, they are decomposed into formic acid, aldehydes, and ketones. Some of them are decomposed on heating with caustic potash. Thus,  $\alpha$ -oxy-isobutyric acid:



Phenyl-lactic acid, heated to only  $130^\circ \text{C}$ ., is decomposed into formic acid and phenyl-aldehyde:



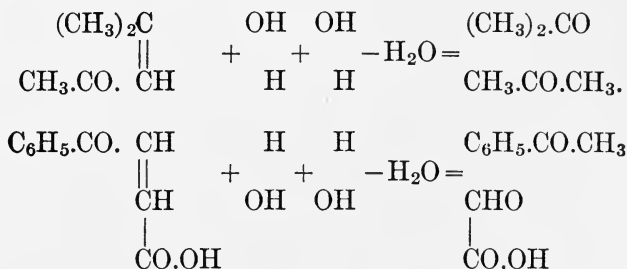
Citric acid is decomposed in an analogous manner, when it is moderately heated with concentrated sulphuric acid, into formic acid and keto-dicarboxylic acid:



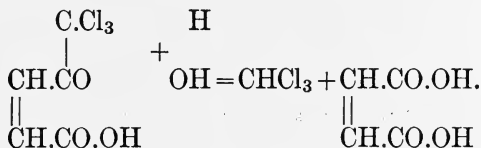
The latter reactions may be regarded as a splitting-off of formic acid.



Unsaturated compounds, by the addition of water (boiling with water, dilute acids or alkalies), can be split at the position of the double link. Mesityl oxide furnishes acetone, and benzoyl-acrylic acid gives aceto-phenone and glyoxylic acid:



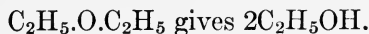
The rupture may also take place at a point other than that of the double link. For instance,  $\beta$ -trichlor-acetyl-acrylic acid, by boiling with baryta-water, is decomposed into chloroform and fumaric acid:



For cases of a rupture of the carbon bonds without a rupture of the molecule, see page 138.

### B. Hydration followed by a Rupture of a Bond between Carbon and Oxygen.

The oxides of alcohol radicals, either the same or different, are decomposed by the fixation of water when they are heated with dilute mineral acids. Thus:



The true esters are only decomposed with difficulty with water alone, and even then but incompletely. In the cold, ethyl acetate,  $\text{CH}_3.\text{CO}.\text{OC}_2\text{H}_5$ , is slightly decomposed by water;

at 100° C., after six hours' boiling, the decomposition is not very great. The saponification takes place more rapidly by the action of acids and caustic alkalies; the latter are mostly employed. The rapidity of the decomposition of the ester depends on its nature, as well as on the acid or alkali employed, and the conditions of the experiment.

To saponify esters they are heated with an excess of potash or soda, baryta, or lime; the oxides of lead and magnesium are also used. To accelerate the reaction, it is sometimes necessary to add alcohol. The end of the reaction is recognized by the disappearance of the ester, which is difficultly soluble in water. If an alkaline solution is used, the alcohol is removed by steam, or by agitation with a suitable solvent. The liquid is then acidulated, and, if the acid does not separate, it is removed by a solvent. If the acid gives a difficultly soluble salt, with a metal precipitable with hydrogen sulphide, such a salt may be prepared and subsequently decomposed by hydrogen sulphide. For acids difficultly soluble in water, their barium salts may be prepared and subsequently decomposed with sulphuric acid.

Esters allow of a convenient method for the preparation of substituted products of the alcohols and acids. Thus, malonic ester,  $\text{CH}_2(\text{CO}.\text{OC}_2\text{H}_5)_2$ , treated with chlorine, is converted into chlor-malonic ester,  $\text{CHCl}(\text{CO}.\text{OC}_2\text{H}_5)_2$ , which is decomposed in the cold by alkalies into chlor-malonic acid,  $\text{CHCl} \begin{smallmatrix} \swarrow \text{CO}.\text{OH} \\ \searrow \text{CO}.\text{OH} \end{smallmatrix}$ , and alcohol; if heat is employed, the hydroxy compound tartaric acid,  $\text{CH}(\text{OH}) \begin{smallmatrix} \swarrow \text{CO}.\text{OH} \\ \searrow \text{CO}.\text{OH} \end{smallmatrix}$ , is formed.

To saponify the esters of the aromatic nitro-acids, it is necessary to dilute acids, for the action of alkalies gives rise to azo compounds.

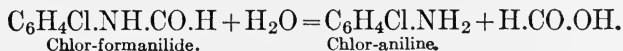
Certain precautions must be taken with ketonic acids; in certain cases, as, for example, with  $\text{C}_6\text{H}_5.\text{CO}.\text{CH}_2.\text{CO}.\text{OC}_2\text{H}_5$ , it is necessary to use sodium carbonate for the saponification, as caustic alkalies cause a more extensive decomposition.

The anhydrides of the carboxylic acids are slowly decomposed by the action of water, and more rapidly by alkalies. The anhydrides of the sulphonic acids are decomposed with a little more difficulty.

The carbohydrates,  $C_{12}H_{22}O_{11}$  and  $C_6H_{10}O_5$ , take up water when heated with dilute acids, and are decomposed into several other carbohydrates. The glucosides are decomposed in the same manner by hydrolysis with dilute acids and the action of certain ferments.

### C. Hydration followed by a Rupture of a Bond between Carbon and Nitrogen.

The substituted derivatives of the amides (anilides), heated in a sealed tube with water or with concentrated acids (HCl and  $H_2SO_4$ ), combine with water and are split up into carboxylic acids and amines:



This reaction is a limited one.<sup>1</sup>

Solutions of alkalies and ammoniacal alcohol react in the same manner, but with more difficulty.

The compounds formed by the action of aldehydes on ammonia and amines (see page 139) are decomposed by hydrolysis (heating with HCl) into their components. Bodies of the formula,  $R.CH=NR'$ , double their molecule when heated with water.

The decomposition of the iso-nitriles into formic acid and amines recalls that of the substituted derivatives of form-anilide.

Alkalies hydrolyze the iso-cyanic esters, and decompose them into carbonic acid and amines. The iso-sulphocyanides

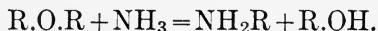
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<sup>1</sup> See Menchoutkine, *Jour. Soc. Phys. Chim. Russe*, vol. 14, p. 274.

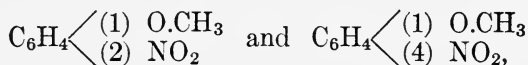
behave in the same manner. Thus,  $\text{C}_6\text{H}_5\text{.NCS}$ , heated with concentrated sulphuric acid (or, for example, hydrochloric acid acting on an alcoholic solution of the body), combines with water and gives  $\text{C}_6\text{H}_5\text{.NH}_2$ , and  $\text{COS}$ .

## II. FIXATION OF AMMONIA.

The decomposition of simple and compound esters by ammonia into amines and alcohols takes place but rarely:



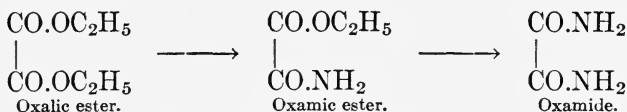
The esters of the ortho- and para-nitrophenols,



heated to  $200^\circ \text{C}$ ., with an aqueous solution of ammonia, give methyl alcohol and the corresponding nitro-anilines.

The true esters of the dicarboxylic acids are decomposed by ammonia into amides and alcohols, and they react with either one or two molecules of ammonia.

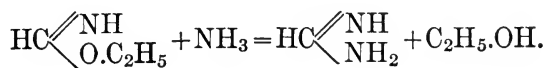
If there be added the theoretical quantity of an alcoholic solution of ammonia to a cooled solution of oxalic ester, there is formed the ester of oxamic acid; with an excess of ammonia, oxamide is obtained:



Ammonia reacts readily with the esters of the substituted acids. When  $\alpha$ -chlor-propionic ester is agitated with ammonia, it is converted into  $\text{CH}_3\text{.CHCl.CO.NH}_2$ . The reaction takes place in the cold, otherwise the chlorine would be replaced by  $\text{NH}_2$ .

The anhydrides of the monobasic acids are decomposed

more or less easily by ammonia with the formation of amides. The imido-esters react very easily with ammonia to form amidines:



## CHAPTER VII.

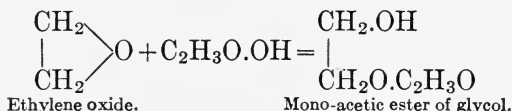
### CONDENSATIONS.

#### I. CONDENSATION BY DIRECT ADDITION.

SOME of the unsaturated hydrocarbons readily combine with acids to form esters of the alcohols. Thus, amylene (trimethyl-ethylene) combines with acetic acid and other acids.<sup>1</sup>

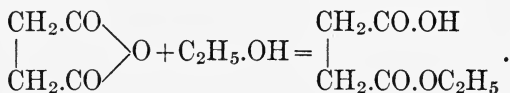
The hydrocarbons,  $C_{10}H_{16}$ , heated with glacial acetic acid, are converted into esters of borneol and its isomerides.

Anhydrides, such as ethylene oxide, easily form with acetic acid esters of the corresponding glycols:

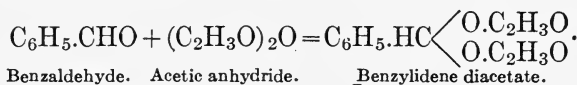


Ethylene oxide also combines with glycol, and even its own molecules polymerize.

The anhydrides of the dibasic acids behave in the same manner. Thus, succinic anhydride, by boiling with absolute alcohol, is converted into the ester of succinic acid:

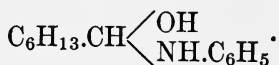


Aldehydes react with the anhydrides and chlorides of the acids to give derivatives of the dihydrates. Thus:



<sup>1</sup> See *Jour. Soc. Phys. Chim. Russe*, vol. 20, p. 594.

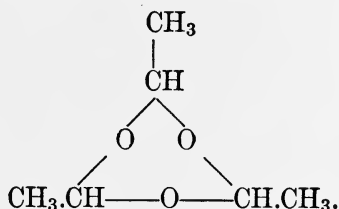
Some aldehydes combine directly with the amines and amides: cœnanthyllic aldehyde with aniline gives a body the formula of which is, undoubtedly,



Ordinary aldehyde gives the following compound with acetamide:



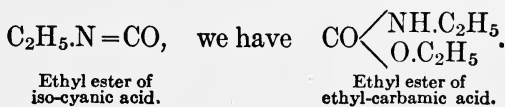
The polymerization of aldehyde can be considered as the combination of several molecules of aldehyde. However, it may also be the result of several reactions (formation at first of a hydrate, then removal of water). Thus, paraldehyde can be represented as the combination of three molecules of the dihydrate united with the loss of  $3\text{H}_2\text{O}$ :



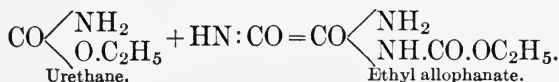
It is possible that the crystalline polymeride of ethylene oxide is formed from glycol in the same manner.

Compounds which contain several atoms of carbon and nitrogen, united with several bonds, generally combine easily with several other molecules.

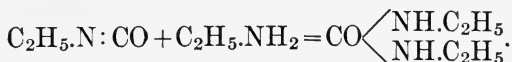
Thus, cyanic acid and the iso-cyanic esters combine with alcohols and various ammonia derivatives. By heating the following ester with ethyl alcohol in sealed tubes to  $100^\circ \text{C}$ .,



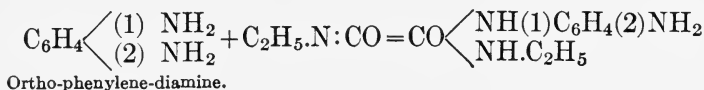
With cyanic acid<sup>1</sup> the reaction takes place in the cold; the carbamic esters (urethanes) formed by the excess of cyanic acid are converted into allophanic esters:



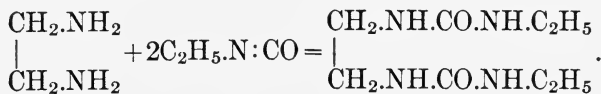
The iso-cyanic esters combine very readily with primary and secondary amines with the formation of substituted derivatives of urea. Thus, iso-cyanic ester is converted into di-ethyl-urea by the action of water, the molecule of ethylamine formed reacting with the ester:



The iso-cyanic esters combine in the same manner with diamines and amides. In the first case, according to the quantity of iso-cyanic ester, there is a combination between one or two molecules:



or:



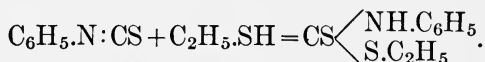
In order to obtain monosubstituted ureas, instead of using free cyanic acid, potassium cyanate may be treated with the salt of the amine; the solution of the two substances in water is evaporated to dryness, and the residue is taken up with alcohol. The cyanate formed in this reaction is converted so rapidly

<sup>1</sup> Therefore, according to this reaction, cyanic acid behaves like a carbimide.



by isomerization into a substituted urea that one cannot be sure of its formation.

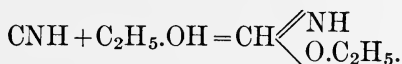
The iso-sulphocyanides, like the iso-cyanic esters, when treated with alcohols and mercaptans, combine with them:



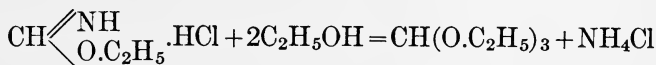
The iso-sulphocyanides also combine with amido compounds, and are converted into derivatives of thio-urea. The reaction proceeds very easily, it being even necessary to moderate it by diluting the reacting bodies with a suitable liquid, alcohol, for example.

Sulphocyanic acid, when treated with amines, gives salts which are much more stable than the corresponding salts of cyanic acid. Thus, sulphocyan-ethyl-amine,  $\text{CNSH.NH}_2.\text{C}_2\text{H}_5$ , does not give ethyl-urea when heated. But the salts of the aromatic amines give the corresponding thio-ureas.

The nitriles combine with alcohols and mercaptans, giving imido-esters and imido-thio-esters. Thus:



The reaction does not occur by the direct combination of the two bodies; it is necessary to pass a current of hydrochloric acid gas through a well-cooled mixture of equi-molecular parts of the two bodies. Under these circumstances there is subsequently formed, with the nitriles of the aliphatic series, a compound of the imido-ester with hydrochloric acid. It is necessary to carefully avoid excess of alcohol, or the following reaction will take place:

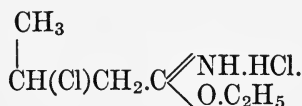


Ortho-formic ester.

In order to decompose the hydrochloric acid compound of the imido-ester, it may be treated with an alcoholic solution

of ammonia, or it may be dissolved in ether and shaken with a solution of caustic soda.

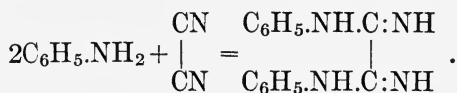
The unsaturated nitriles take up HCl at the same time they form imido-esters. Thus, allyl-cyanide,  $\begin{array}{c} \text{CH}_2 \\ || \\ \text{CH}.\text{CH}_2.\text{CN} \end{array}$ , treated with alcohol and HCl, gives



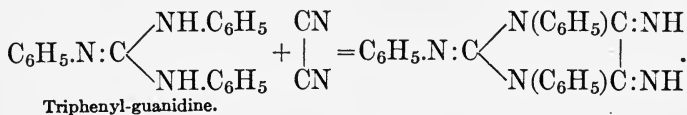
The nitriles combine with amines to form substituted derivatives of the amidines. The reaction is brought about by heating the nitrile with a salt of the amine in a sealed tube:



Cyanogen (nitrile of oxalic acid) reacts at the ordinary temperature with amine compounds. Two  $\text{NH}_2$  groups enter into the reaction; that is to say, two molecules of a mono-amine and a single molecule of a body containing two  $\text{NH}_2$  or  $\text{NH}$  groups. Thus, by passing cyanogen into an alcoholic or ethereal solution of aniline, two molecules of the latter combine with one molecule of cyanogen:

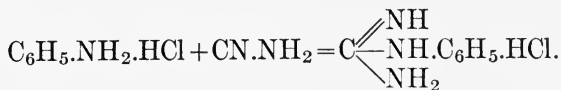


But if a compound containing two  $\text{NH}$  groups is taken, the equation becomes:

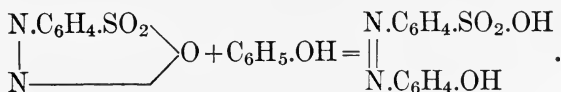


The reaction of CN.CN with amido-benzoic acid takes place between an equal number of molecules.

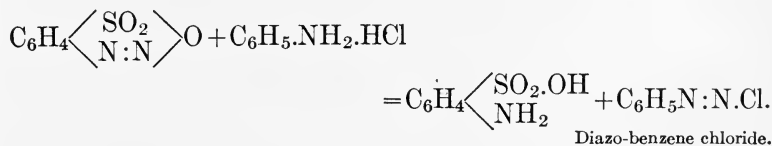
Cyanimide and its derivatives behave like a nitrile, and in reacting with amido compounds they yield derivatives of guanidine. Thus:



The diazo derivatives of the amido-sulphonic acids, by reacting with phenols, oxycarboxylic acids, or amido derivatives, form azo compounds (azo-colors). Thus:

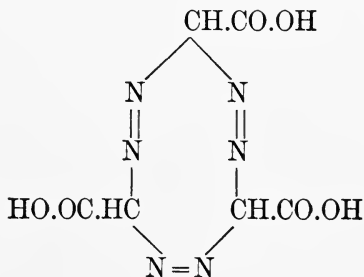


The reaction is carried out by taking the theoretical quantity of the diazo compound prepared in advance, or the end product of the action of sodium nitrite on sulphanilic acid,  $\text{C}_6\text{H}_4 \begin{array}{l} \text{NH}_2 \\ \text{SO}_3\text{H} \end{array}$ , which is added to a strongly alkaline solution of phenol; the intermediate compound which is formed can be transformed by acetic acid into  $\text{HO}.\text{C}_6\text{H}_4.\text{N}:\text{N}.\text{C}_6\text{H}_4.\text{SO}_2.\text{OK}$ . In using amines, it is better to take the hydrochloric acid salts. Other products are also obtained at the same time, according to the equation:



The action of ammonia, or of a concentrated solution of potash at 100° C., on diazo-acetic esters, offers an interesting case of condensation. Under these conditions there is obtained

a salt (or an amide) of three times the molecular weight of diazo-acetic acid ( $\text{CHN:N.CO.OH}$ )<sub>3</sub>, which no doubt has the formula:

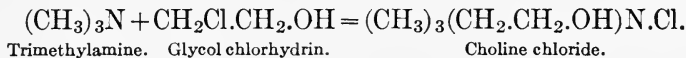


The triazo-acid is decomposed by acids with the formation of diamide (hydrazine), formic, and carbonic acids:



On heating, it loses water of crystallization, and then carbonic acid, and is converted into a body having the formula,  $\text{C}_3\text{H}_6\text{N}_6$ .

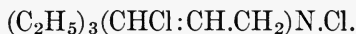
Tertiary amines combine with various chlorinated bodies, with the formation of ammonium derivatives:



Trimethylamine. Glycol chlorhydrin.

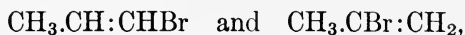
Choline chloride.

If the chlorinated derivative contains several atoms of chlorine, sometimes there may be a removal of halogen acid. Thus, by the action of glycerine trichlorhydrin on triethylamine, there is formed the ammonium compound:



The splitting-off of halogen acid takes place also when the halogen is attached to a carbon atom connected with a

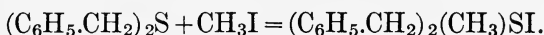
neighboring atom with a double link, as in the case of the propylene bromides,



which, with triethylamine, give allylene,  $\text{CH}_3.\text{C}\equiv\text{CH}$ , and triethylamine hydrobromide.

The halogenated compounds of the secondary and tertiary alcohol groups do not combine with amines, but are decomposed into hydrocarbons and halogen acids.

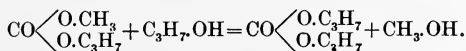
The sulphur derivatives of the formula,  $\text{R}_2\text{S}$ , combine with bromine and iodine compounds:<sup>1</sup>



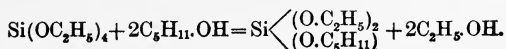
The body  $(\text{C}_5\text{H}_{11})(\text{C}_2\text{H}_5)\text{S}$ , heated with methyl iodide, does not give a compound containing three different groups, but  $(\text{CH}_3)_3\text{SI}$ , the  $\text{CH}_3$  groups displacing  $\text{C}_2\text{H}_5$  and  $\text{C}_5\text{H}_{11}$ . The same result is obtained if triethyl-sulphine iodide,  $(\text{C}_2\text{H}_5)_3\text{SI}$ , is heated with methyl iodide; there is obtained trimethyl-sulphine iodide,<sup>2</sup>  $(\text{CH}_3)_3\text{SI}$ .

<sup>1</sup> For the valency of sulphur, see *Gazz. chim. ital.*, vol. 18, p. 62.

<sup>2</sup> An analogous substitution by the methyl group takes place in the action of methyl alcohol on nitrous ester (*Gazz. chim. ital.*, vol. 12, p. 435). In some cases, on the contrary, the methyl group is displaced by a radical containing more carbon atoms:



In the same manner the ethyl group is displaced by the amyl group in the silicic esters:



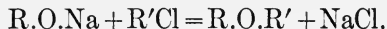
## II. CONDENSATION BY DOUBLE DECOMPOSITION, OR BY REMOVAL OF GROUPS.

### A. Formation of Ethers and Analogous Bodies.

#### (1) With the Liberation of a Mineral Acid or of a Salt.—

It is in this manner that ordinary ether is formed when ethyl bromide or iodide is heated with water, or alcohol with hydrochloric acid at 240° C. In the former case the alcohol formed at first reacts on the halogen compound; and, in the second case, the ethyl chloride which is formed reacts on the alcohol. Sulphuric acid with alcohol also produces ether (the ordinary method of producing this compound).

In order to obtain mixed ethers (the tertiary alcohols of the aliphatic series do not yield any), very often recourse is had to the action of halogen derivatives on the metallic compounds of the alcohols (alcoholates and phenates):



To a solution of sodium alcoholate in alcohol (by dissolving sodium in alcohol) there is directly added the theoretical quantity of the halogen compound, and the reaction is finished by heating; or the alcoholate may be isolated by distilling off the alcohol, and then it is allowed to react with the halogen compound. The phenates, obtained by evaporation of an alkaline solution of phenol, are treated with the halogen compound or with alkyl acid sulphate.

The simple or mixed ethers can also be prepared by heating (in a sealed tube if necessary) together potash, alcohol, and the halogen compound.<sup>1</sup>

With the aliphatic alcohols there are often formed unsaturated hydrocarbons as secondary products.

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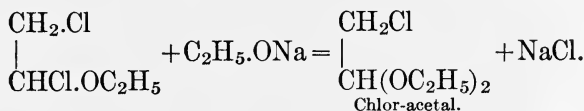
<sup>1</sup> To obtain the ethers of phenols the alcohol is added, together with the corresponding hydrochloric acid ester.

Compounds rich in hydroxyl groups readily give several ethers, principally the neutral ethers. Hydroquinone, on boiling with an excess of potash and methyl iodide, gives dimethyl ether; glycerin, with propyl iodide and potash, furnishes  $C_3H_5(OC_3H_7)_3$ .

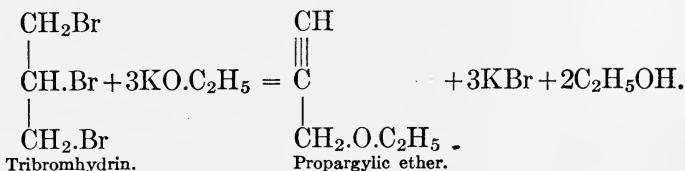
In order to substitute only a part of the hydroxyl groups, it is necessary to take the theoretical quantities of potash and RI or sulphovinate.

Even when oxycarboxylic acids, oxyaldehydes, and other compounds containing the OH group, are heated with potash and RI or R.OH, they are converted into the corresponding ester.

Bodies rich in halogen react with several molecules of alcoholates. Thus, ethylidene bromide,  $CH_3.CHBr_2$ , is converted into acetal (ether of a dihydrate), and chloroform into orthoformic ether (ether of a trihydrate). If the halogen atoms are not fixed to one and the same carbon atom, but to neighboring atoms, there may be partial or total substitution:



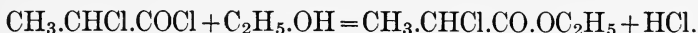
There may be a simultaneous splitting-off of halogen acid. The tribromhydrin of glycerin, by the action of a solution of caustic potash in alcohol, gives the ether of propargylic alcohol:



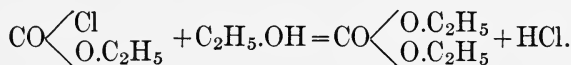
To the reactions above enumerated must be added that between a halogen compound, RI in particular, and a metallic oxide,  $M_2O$ . Generally, silver oxide is used; sometimes there

may be a removal of hydriodic acid and a replacement of I by OH.<sup>1</sup>

The true esters are obtained very easily by the action of acid chlorides, which readily react with OH groups. The chlor-acid chlorides behave in the same manner:



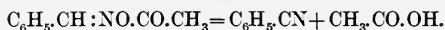
In this reaction it is only the chlorine of the CO.Cl group which reacts. The chloride of chlor-formic acid (carbonyl chloride, COCl<sub>2</sub>) does not give the same reactions on account of its particular constitution; with alcohol in the cold, it gives esters of chlor-formic acid, which, by boiling with alcohols, are converted into esters of carbonic acid:



The chlorides of the dicarboxylic acids exchange only one of their chlorine atoms for OR.

Compounds containing several OH groups will react with several molecules of acid chlorides.<sup>2</sup> In the aliphatic series, the hydrochloric acid which is liberated can also enter into

<sup>1</sup> By the use of acid chlorides the hydrogen of the hydroxyl group of oximes may also be replaced. Thus, acetoxime (CH<sub>3</sub>)<sub>2</sub>C:N.OH, with benzoyl chloride, gives (CH<sub>3</sub>)<sub>2</sub>C:N.O.CO.C<sub>6</sub>H<sub>5</sub>. From the aldoximes may readily be obtained the acids of which they consist, through often, in their place, decomposition products are formed:

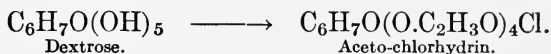


In the oximes, the hydrogen of the hydroxyl group may easily be replaced by an alcoholic radical. If benzaldoxime and CH<sub>3</sub>I are added to an alcoholic solution of caustic soda, there is formed C<sub>6</sub>H<sub>5</sub>.CH:NO.CH<sub>3</sub>.

<sup>2</sup> The reaction with the acid chlorides, particularly C<sub>6</sub>H<sub>5</sub>.CO.Cl, is a means of determining the presence of the hydroxyl (OH) group. The product of the reaction, freed from excess of benzoyl chloride, is decomposed with standard potash, and the excess of the latter determined by titration.



the reaction and convert OH into Cl. Dextrose with acetyl chloride gives an aceto-chlorhydrin:<sup>1</sup>

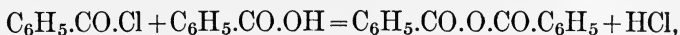


In certain cases, in order to obtain the esters the acid chloride is allowed to act on an alcoholate.<sup>2</sup> Thus, the esters of cyanic acid,  $\text{N}\equiv\text{C}.\text{OC}_2\text{H}_5$ , are obtained by the action of cyanogen chloride on an alcoholate dissolved in an excess of alcohol.

The esters are also formed by the reaction of the salts of the carboxyl acids (and, in the same manner, the thio-acids) and their derivatives with halogen compounds.<sup>3</sup> Generally, the chlorine or bromine compound is allowed to react on the alkaline salt of the acid, or the iodine derivative on the silver salt.

The silver salt, moistened with the corresponding acid, is gradually heated with RI; a certain quantity of the product escapes during the reaction, but this may be avoided by taking an excess of silver salt. In certain cases it is necessary to dilute the reagents in ether in order to moderate the reaction.

The anhydrides of the acids are obtained with difficulty by the action of acid chlorides on the acids. Thus, the reaction,



only takes place by heating in a sealed tube, and even, in any case, only about 50 per cent. of the theoretical yield is obtained.

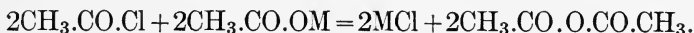
<sup>1</sup> See A. Colley, *On Grape Sugar*, Moscow, 1869 (in Russian).

<sup>2</sup> The chlorides of the sulphonic acids,  $\text{R}.\text{SO}_2.\text{Cl}$ , behave like those of the carboxylic acids; with alcohols and the alcoholates they yield the corresponding esters. Sometimes it is sufficient to evaporate the alcoholic solution to obtain the ester; but in other cases, a prolonged boiling is required or zinc dust is used, as, for example, in the reaction of  $\text{R}.\text{SO}_2.\text{Cl}$  on the phenols. The action of the chloride of the sulphonic acids may be moderated (particularly  $\text{C}_6\text{H}_5.\text{SO}_2.\text{Cl}$ ) by dissolving them in ether, or by adding the alcoholate in an excess of alcohol.

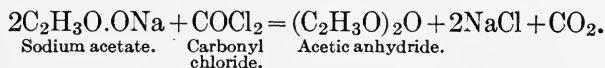
<sup>3</sup> In the same manner are produced the esters of the dihydric alcohols. See I. Tuttschew, *On Glycols in General and on a New Compound, Carvol-dibenzoate*, St. Petersburg, 1858 (in Russian).

A good method of obtaining the anhydrides is the action of dehydrated oxalic acid on acid chlorides, or the action of the latter on the salt of the acid.<sup>1</sup>

In place of using the ready-prepared chloride, the direct action of phosphorus oxychloride (1 molecule) on the salt of the acid (4 molecules) may be used. The reaction takes place in two phases:



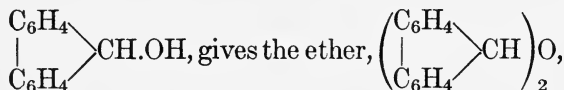
The anhydrides of the acids are also obtained by the action of the acid chloride on the nitrate of lead or silver, and also by the action of carbonyl chloride on the sodium salt of the acid:



**(2) Formation of Ethers, etc., with Liberation of Water.—**

The direct formation of simple or mixed ethers (oxides of the alcoholic radicals), with elimination of water, takes place only with difficulty and always incompletely. With ethyl alcohol, the ether is obtained by energetic heating with a sulphate or a chloride, although it may be considered that the ether is formed through the action of the acid liberated in the decomposition of the salt.

Benzhydrol,  $(\text{C}_6\text{H}_5)_2.\text{CH}.\text{OH}$ , is readily converted into the corresponding ether,  $[(\text{C}_6\text{H}_5)_2\text{CH}]_2\text{O}$ ; the alcohol of fluorene,



by simple fusion; the alcohol of cumene,  $\text{C}_6\text{H}_4(\text{C}_3\text{H}_7)\text{CH}_2.\text{OH}$ , containing traces of inorganic substances (one or two drops of

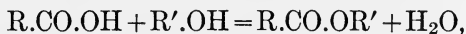
<sup>1</sup> With the chlorides of the polycarboxylic acids there may be a secondary reaction on account of the splitting off of water.

sulphuric acid, for example), is decomposed on distilling into the ether  $[\text{C}_6\text{H}_4(\text{C}_3\text{H}_7)\text{CH}_2]_2\text{O}$  and water. (For the ethers of the dihydrates, see previous pages.)

The methods employed in the aliphatic series do not always hold with the phenols, and it is necessary to use dehydrating agents. Thus phenol, heated with zinc chloride, gives a small quantity of the ether  $(\text{C}_6\text{H}_5)_2\text{O}$ . Resorcin, at  $180^\circ \text{C}$ ., with fuming hydrochloric acid, gives the corresponding ether of resorcin,  $(\text{C}_6\text{H}_4.\text{OH})_2\text{O}$ .

The anhydrides of the mono carboxylic acids are obtained with difficulty, even by the action of strong dehydrating agents. Glacial acetic acid with phosphoric anhydride gives a small quantity of acetic anhydride. For its preparation there may be employed an iso-nitrile (see page 138).

The formation of the esters by the use of alcohols and acids takes place much better, but the reaction,



is never complete; as soon as there is an equilibrium established between the decomposition of the acid ester and the water on the one hand, and the formation of the ester on the other hand, the reaction stops.

The point of equilibrium depends on the nature of the alcohol and ester. It is necessary to use an excess of the reagents and to remove the water which is formed at the same time as the ester. This is usually accomplished by passing a current of dry hydrochloric acid gas through a mixture of the alcohol and acid, and heating from time to time.

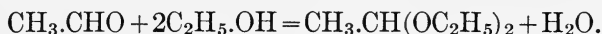
The esters of the phenols are formed by the action of phosphorus oxychloride on a mixture of the phenol and acid, there being a liberation of hydrochloric acid.

With polyhydric alcohols, according to circumstances, it is possible to replace one or more hydrogen atoms of the OH groups.

The anhydrides of the acids react more readily than the

acids with alcohols, even without heating and in the absence of dehydrating agents; and in the majority of cases the reaction is complete. They are employed in the preparation of esters to replace the acid chlorides when the latter react with difficulty or give secondary products. In the case of acetic anhydride, its action is increased by the addition of dehydrated sodium acetate.

The acetals (ethers of the dihydrates) are obtained by heating aldehydes with alcohols:



The reaction takes place at  $100^\circ \text{C}.$ , if to a mixture of the aldehyde (1 part), and the alcohol (3 parts), there is added glacial acetic acid ( $\frac{1}{2}$  part); as a secondary product there is formed some acetic ester, which is removed by heating in a closed vessel with caustic potash; the acetal formed being dehydrated with calcium chloride. A better yield of acetal is obtained by passing a current of non-inflammable hydrogen phosphide into a mixture of alcohol and aldehyde, cooled to  $21^\circ \text{C}.$

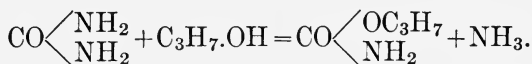
The polyhydric alcohols behave in the same manner with aldehydes as the monohydric alcohols.

Acetals are generally obtained by the oxidation of the corresponding alcohols.<sup>1</sup>

**(3) Formation of Esters, etc., with Liberation of Ammonia or Nitrogen.**—The amides of certain acids can be converted into esters with liberation of ammonia by the action of alcohols in the presence of acids. Thus:



By boiling urea with a large quantity of propyl alcohol, we have:

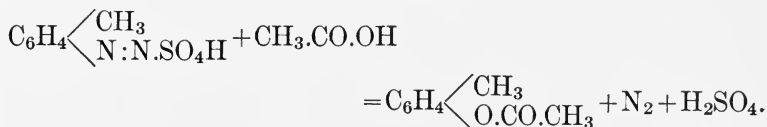



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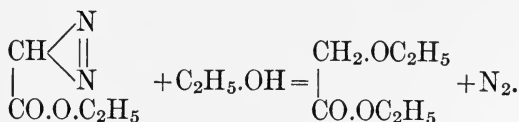
<sup>1</sup> By the oxidation of a mixture of methyl and ethyl alcohols, there is obtained, not the mixed acetal,  $\text{CH}_3.\text{CH}(\text{OCH}_3)(\text{OC}_2\text{H}_5)$ , but a mixture of methyl and ethyl acetals.

For the preparation of ortho-esters (ortho-formic ester), by the reaction of imide-ethers on alcohols, see page 153.

The diazo-compounds may be converted into esters under certain conditions. Thus, by decomposing the aromatic diazo-derivatives with acetic acid, the acetic esters of the phenols are obtained:

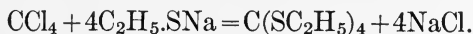


The esters of diazo-acetic acid, on boiling with alcohol, give the esters of ethyl-glycolic acid:



### B. Preparation of Compounds containing Sulphur.

Sulphuretted compounds may be obtained by the action of chlorine compounds (or salts of the sulphonic acids) with the corresponding mercaptides,  $\text{RSM}^1$ :



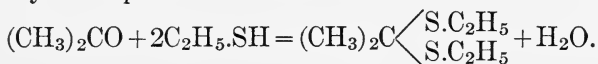
Sulphuretted compounds containing two similar R groups are obtained directly by the action of the chlorine compounds on potassium sulphide,  $\text{K}_2\text{S}$ .

The tertiary halogen derivatives, as, for example, tertiary iso-butyl iodide  $(\text{CH}_3)_3\text{C} \cdot \text{I}$ , do not form sulphur compounds with potassium sulphide, for generally there is a decomposition of the halogen compounds. Among the aromatic halogen deriva-

<sup>1</sup> The acid chlorides react with the mercaptans themselves. Thus,  $\text{C}_2\text{H}_5 \cdot \text{SH}$  heated with acetyl chloride,  $\text{CH}_3 \cdot \text{CO} \cdot \text{Cl}$ , liberates hydrochloric acid and gives the ester of thioacetic acid,  $\text{CH}_3 \cdot \text{CO} \cdot \text{S} \cdot \text{C}_2\text{H}_5$ .

tives there are some in which the halogen is replaced by HS by treatment with potassium sulphide.

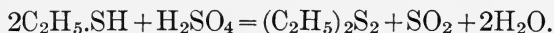
Sulphur compounds similar to those of the dihydrates are formed by the condensation of aldehydes and ketones with mercaptans and thio-glycollic acid. By passing hydrochloric acid into a mixture of mercaptan and acetone, there is formed aceto-ethylmercaptol:<sup>1</sup>



Compounds containing  $\text{S}_2$  are formed by the action of halogen compounds on  $\text{M}_2\text{S}_2$ ; and by the removal of hydrogen from mercaptans and thio-acids with the aid of oxidizing agents (gaseous oxygen, ferric chloride, chromic and nitric acids, hydrogen peroxide, etc.); thus:

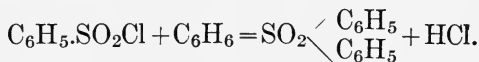


The preparation of compounds containing  $\text{S}_2$ , by the action of sulphuric acid on mercaptans, takes place according to the following equation:



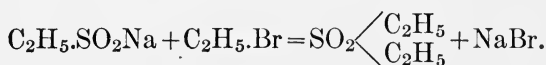
By the action of iodine on  $\text{C}_2\text{H}_5\cdot\text{SNa}$ , the disulphide of phenyl,  $(\text{C}_6\text{H}_5)_2\text{S}_2$ , is formed.

The sulphones,  $\text{R}\cdot\text{SO}_2\cdot\text{R}$ , are formed by heating an aromatic sulphonic acid with an aromatic hydrocarbon in the presence of a dehydrating agent, such as phosphoric anhydride; they are also obtained by the action of sulphuric anhydride on a hydrocarbon, and by the action of sulphochlorides or aromatic hydrocarbons in the presence of aluminium chloride. Thus:



<sup>1</sup> By oxidizing with potassium permanganate there is formed a disulphone,  $(\text{CH}_3)_2\text{C}(\text{SO}_2\cdot\text{C}_2\text{H}_5)_2$ , called sulphonol, which has a physiological action somewhat analogous to chloral.

The sulphones are also obtained by the action of halogen compounds on the salts of the sulphinic acids:



For the preparation of sulphones by the oxidation of sulphur compounds, see under direct fixation of oxygen.

### C. Formation of Compounds containing Nitrogen.

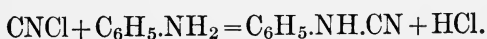
#### (1) AMMONIA DERIVATIVES.

(a) **Derivatives formed with Liberation of Halogen Acids or other Acids or Salts.**—The amines react with halogen compounds in the same manner as ammonia (see page 93), and are converted into secondary amines, and even tertiary amines, with an excess of the halogen compound.

The secondary iodides, in their action on amines, yield hydrocarbons together with secondary amines. For example, isopropyl-iodide  $(\text{CH}_3)_2\text{CH}\cdot\text{I}$ , with isopropyl-amine  $(\text{CH}_3)_2\text{CH}\cdot\text{NH}_2$ , is converted into  $[(\text{CH}_3)_2\text{CH}]_2\cdot\text{NH}$  and propylene,  $\text{CH}_3\cdot\text{CH}:\text{CH}_2$ . In order to separate the substances so formed, the mixture is treated with nitrous acid, and, by the nitrosamine thus produced, the secondary amine is removed.

The amido-acids react with chlorine compounds, and, according to the conditions of the reaction, there is a substitution of one or two atoms of hydrogen in the  $\text{NH}_2$  group. By heating one molecule of para-amido-benzoic acid,  $\text{C}_6\text{H}_4 \begin{matrix} \diagup (1) \text{NH}_2 \\ \diagdown (4) \text{CO}\cdot\text{OH} \end{matrix}$  with a solution (3 mols.) of caustic soda in alcohol and two molecules of methyl iodide, there is obtained dimethyl-para-amido-benzoic acid,  $\text{C}_6\text{H}_4 \begin{matrix} \diagup (1) \text{N}(\text{CH}_3)_2 \\ \diagdown (4) \text{CO}\cdot\text{OH} \end{matrix}$ .

Amines with cyanogen chloride give substituted cyanamines. The reaction is brought about by passing cyanogen chloride into an ethereal solution of the amine:



With an excess of amine, a guanidine substitution product is formed.

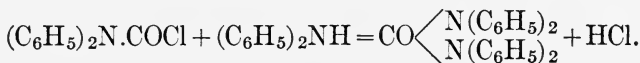
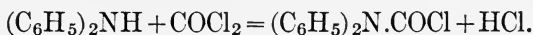
The acid chlorides react energetically with amido compounds, as do also the sulpho-chlorides,  $R.SO_2.Cl$ :



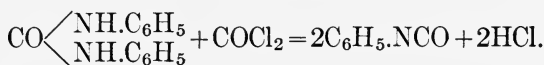
The substituted amides so formed (for example, the anilides) do not present a basic character.

As to the manner in which the acid chlorides behave with ortho-diamines, see page 117.

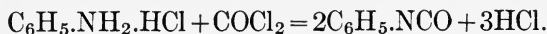
Carbonyl chloride,  $COCl_2$ , with secondary diamines, behaves in the same manner as other acid chlorides; there is a substitution of H by  $COCl$ , and the formation of special chlorides derived from urea, which in their turn, when heated with the diamine, give substituted derivatives of urea. Thus:



The primary amines of the aromatic series yield disubstituted ureas, which in their turn, when heated a long time with carbonyl chloride, give isocyanic esters:



Phenyl-isocyanate,  $C_6H_5.NCO$ , may be obtained in the same direct manner by passing carbonyl chloride over the fused chloride of the amine:

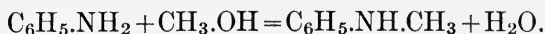


In the aliphatic series, the isocyanic esters are obtained by the distillation of  $RI$  or  $R.HSO_4$  with the cyanates.



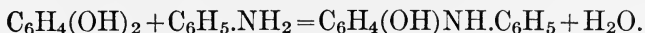
**(b) Ammonia Derivatives formed with Liberation of Water.**

—The primary aromatic amines become secondary, and the secondary tertiary, when they are heated with alcohols of the aliphatic series. Thus:

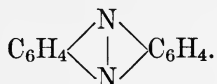


The higher alcohols of the aliphatic series, with dehydrating agents, give substituted derivatives of the R group in the hydrogen of the benzene nucleus.

The phenols react with the amines when heated to 250–300° C. in the presence of the chlorides of zinc or calcium. The diphenols react more readily; for example, resorcin or hydroquinone with aniline react at 300° C. with dehydrating agents:



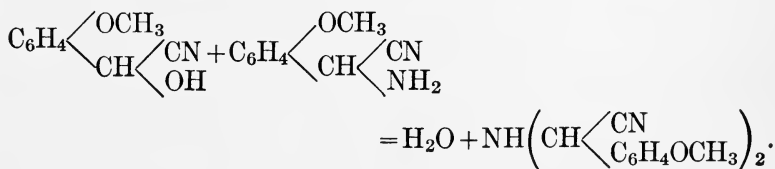
With ortho-diamines, pyrocatechin gives phenazines; for example, when heated for some time with ortho-phenylenediamine, it gives the phenazine identical with the azo-phenylene,  $\text{C}_{12}\text{H}_8\text{N}_2$ , of Rasenack and Claus:



In this case, there is a removal of  $\text{H}_2$  at the same time as a removal of water.

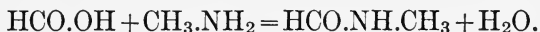
The  $\alpha$ -oxynitriles react easily with amido compounds.

If the cyanhydrate of methyl-salicyl aldehyde is heated with an alcoholic solution of ammonia to 60–70° C., there is at first obtained the nitrile of an amido-acid, which then reacts again on the cyanhydrin in excess, as indicated by the following:



The carboxylic acids readily react with amines to form at first salts, which by loss of water give substituted amines.

If an aqueous solution of methylamine and formic acid is distilled, there is formed methyl-formamide:



Benzyl-acetamide is obtained by heating benzylamine with glacial acetic acid; acetanilide is obtained by a similar process<sup>1</sup> (see page 175). By heating equal molecules of acid and amine the reaction is not complete, for the water formed causes the decomposition of the substituted derivatives of the amine (see page 147); in order to increase the yield, it is necessary to take an excess of acid. In certain cases, the reaction is made more complete by heating in sealed tubes, or by the use of dehydrating agents. For example, in order to prepare chlor-acetanilide, the chlor-acetate of aniline is treated with phosphoric anhydride:



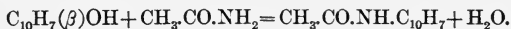
Without this assistance there would probably be formed phenylglycocoll,  $\text{CH}_2(\text{NH.C}_6\text{H}_5)\text{CO.OH}$ , with liberation of hydrochloric acid.

Diamido compounds react with either one or two molecules of acid.

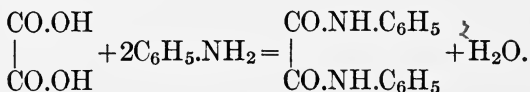
For the manner in which the ortho-diamines behave with acids, see page 117.

Dicarboxylic acids form two series of derivatives, according to the number of molecules taking place in the reaction. By

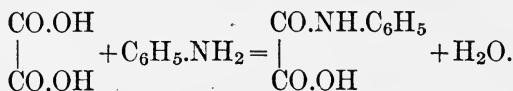
<sup>1</sup> The substituted derivatives of the amides can be obtained by the action of the amines on the esters, alcohol being liberated. The substituted derivatives of the aromatic amines (anilides) are formed in some cases by the action of phenol on the amine:



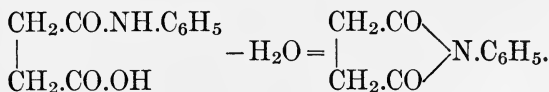
heating aniline with an excess of oxalic acid, the derivatives of oxamide are obtained:



With equal molecules of acid and base, a derivative of oxamic acid is formed:

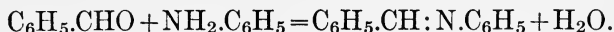


Some substituted derivatives of the amido-acids at the temperature at which they are formed decompose into water and a substituted derivative of an imide:



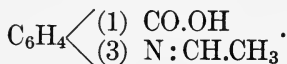
The anhydrides of the acids behave in the same manner as the acids when treated with amines. They are used when the  $\text{NH}_2$  group is substituted with difficulty in the acid radical, or when it is necessary to avoid a long heating, which is necessary when the acid is used. The reaction with anhydrides can be moderated by using a suitable solvent, or it may be increased by means of a dehydrating agent, such as fused sodium acetate. With amido-phenol, the acid group of the anhydride does not only act on the  $\text{NH}_2$  group, but also on the  $\text{OH}$  (see page 164). For ortho-amido-phenol, see page 117.

The aldehydes react with one or two molecules of amido compounds, with the liberation of water and the formation of a single or double bond between the carbon and nitrogen.<sup>1</sup> Thus benzaldehydes react with aniline as follows:



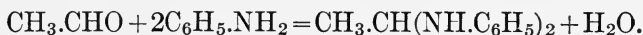
<sup>1</sup> For the action of aldehydes on aromatic amines, see p. 196.

Ordinary aldehyde behaves in the same manner with meta-amido-benzoic acid, forming:

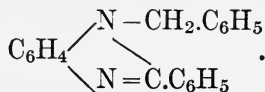


There may at first be formed an addition product,  $\text{R.CH(OH).NH.R'}$  (see page 151), which is then decomposed with loss of water.

Ordinary aldehydes react with two molecules of primary or secondary amines.<sup>1</sup> On mixing one molecule of aldehyde with two molecules of aniline, the following reaction takes place:



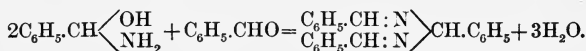
The aromatic aldehydes condense with ortho-diamines with liberation of  $2\text{H}_2\text{O}$  (2 mols. of aldehyde and 1 mol. of ortho-diamine). The compound so formed is not a simple substitution of the hydrogen of the ammonia by  $2\text{R}''$ ; it is called *aldehydine*, and is a derivative of the amidines (see page 154). Thus, by the action of benzaldehyde on ortho-phenylenediamine, we obtain benzaldehydine:



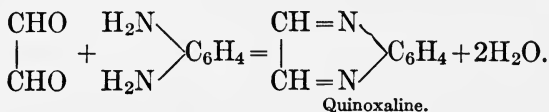
In this reaction there is a simultaneous reduction and oxidation of benzaldehyde.

Glyoxal, and compounds containing two CO groups in

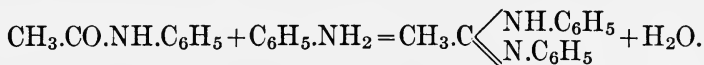
<sup>1</sup> The formation of such compounds as ammonia-acrolein and hydrobenzamide can be explained by admitting that they are the result of a condensation between the aldehyde and the addition products of ammonia:



the ortho position (benzil, phenanthraquinone, etc.), combine with ortho-diamines to give *quinoxalines*:<sup>1</sup>



Bodies containing the CO group react in the same manner as aldehydes<sup>2</sup> with bodies containing NH<sub>2</sub>. The anilides, heated with amines and phosphorus trichloride, give substituted derivatives of the amidines:



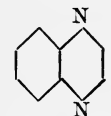
As the anilide is prepared by the action of the acid on the amine, it is possible to obtain the substituted derivatives of the amidines by heating together the amine and acid with phosphorus trichloride.

Urea condenses (with liberation of water) with various compounds. By heating it with isodialuric acid (obtained by the conversion of the condensation product of aceto-acetic

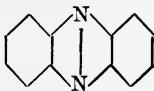
<sup>1</sup> Hinsberg (*Annalen*, vol. 237, p. 327) reserves the name of quinoxalines to compounds which contain the nucleus:



at the end of a chain of hexagonal nuclei, and gives the name of *azines* to those which contain the same nucleus in the middle of such a chain:



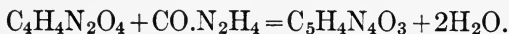
Quinoxaline.



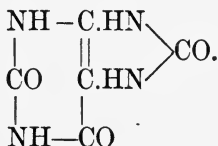
Azine (diphenazine).

<sup>2</sup> For the condensation of amines with carbohydrates, see W. Sorokine, *Action of Glucose on Aniline and Toluidine*, Kasan, 1887 (in Russian).

ester with urea) and concentrated sulphuric acid, uric acid is produced:<sup>1</sup>

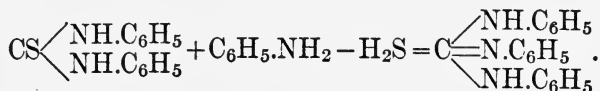


The formation of uric acid under these conditions leads to the following formula for this body:



(c) **Ammonia Derivatives formed with Liberation of H<sub>2</sub>S.**—

Bodies containing the CS group react with amines in the same manner as bodies containing CO. Thus, diphenyl-thio-urea in alcoholic solution condenses with aniline in the presence of a metallic oxide to yield triphenyl-guanidine:



Carbon disulphide with aromatic amines gives substituted derivatives of thio-urea with liberation of hydrogen sulphide. Thus aniline heated with carbon disulphide and alcohol (with an inverted condenser) gives

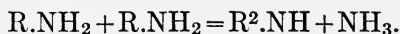


For the action of carbon disulphide on the aliphatic amines, see under removal of hydrogen sulphide.

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<sup>1</sup> See *Annalen*, vol. 251, p. 235.

(d) **Ammonia Derivatives formed with Liberation of  $\text{NH}_3$ .**—The primary amines, on heating, are frequently converted into secondary amines:



This reaction is facilitated by adding some substance capable of absorbing ammonia, such as calcium chloride or zinc chloride, or acids.

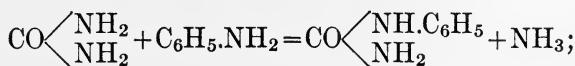
Dianthramine is readily formed by heating anthramine,  $\text{C}_{14}\text{H}_9\text{NH}_2$ , with boiling glacial acetic acid; as a secondary product there is formed aceto-anthramine:



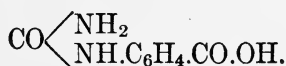
The best method of obtaining certain secondary amines is to heat the amine with its hydrochloride:



In this manner secondary amines may be obtained with different radicals, and also secondary acid amides. The reaction between an amine and an acid amide takes place readily. If acetamide is heated with aniline until ammonia is no longer disengaged, acetanilide is obtained in theoretical amount. Urea behaves in the same manner; heated with aniline or its hydrochloride, it gives phenyl-urea:



fused with an excess of meta-amido-benzoic acid, it gives uramido-benzoic acid:



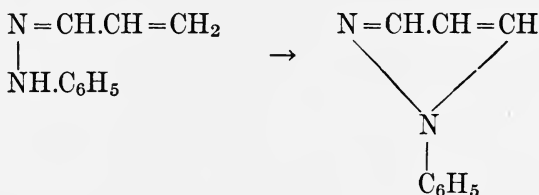
With an excess of amine, urea gives disubstituted ureas. In some cases the NH group of amidines react with amines; for example:



(2) DERIVATIVES OF THE DIAMINES  $\text{R}(\text{NH}_2)_2$  AND THE DIIMIDES  $\text{R}(\text{NH})_2$ .

(a) **Substituted Hydrazines.**—The hydrazine substitution products (symmetrical) are obtained from phenylhydrazine by the action of bromine compounds, acid chlorides, acid anhydrides, and acid amides.

Phenylhydrazine condenses with aldehydes and ketones with liberation of water, this being a characteristic reaction for this body. With benzaldehyde, for example, it gives  $\text{C}_6\text{H}_5.\text{CH}:\text{N}.\text{NH}.\text{C}_6\text{H}_5$ .<sup>1</sup> The unsaturated aldehydes and ketones give hydrazine derivatives, which on distillation lose  $\text{H}_2$  and are converted into pyrazol derivatives. Thus, the product of the reaction of acrolein on phenylhydrazine gives phenylpyrazol:




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<sup>1</sup> Glucose, like the aldehydes, reacts in the cold with one molecule of phenylhydrazine with liberation of water. On heating with phenylhydrazine, two molecules enter into reaction, and a yellow precipitate is formed. The reaction may be represented by the equation:



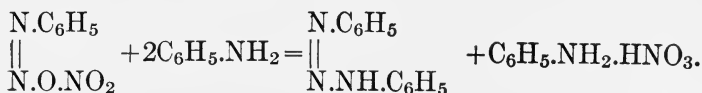
It is interesting to know that, through this compound, dextrose may be converted into lævulose; on reduction of the hydrazine derivative, there is formed iso-glucosamine,  $\text{C}_6\text{H}_{11}(\text{NH}_2)\text{O}_5$ , and this, by treatment with nitrous acid, is completely converted into lævulose.



Among the derivatives of pyrazol is found antipyrine (used as a febrifuge and analgesic), which is obtained by the condensation of aceto-acetic ester with methyl-phenyl-hydrazine (symmetrical) with liberation of water and alcohol,  $C_2H_5.OH$ .

For derivatives of phenylhydrazine, see page 179.

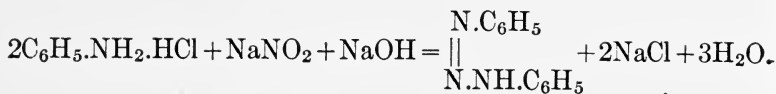
(b) **Diazo-amido Compounds.**—On mixing the aqueous or alcoholic solutions of a diazo-salt and an amido compound, there is formed a diazo-amido body:



If the diazo-salt and the primary amine contain different radicals, there are formed diazo-amides which are identical whether  $R.N:N.Cl$  reacts on  $R'NH_2$  or  $R'N:N.Cl$  on  $R.NH_2$ . But in the case of secondary amines, under the same conditions, there will be formed two different isomers. Thus, by the action of diazobenzene chloride,  $C_6H_5.N:N.Cl$ , on mono-ethyl-toluidine,  $C_6H_4(CH_3)NH.C_2H_5$ , a body is formed which shows different properties and decomposition products from that formed by the action of diazo-toluene chloride,  $C_6H_4.(CH_3)N:N.Cl$ , on ethyl-aniline,  $C_6H_5.NH.C_2H_5$ .

The formation of diazo-amido derivatives by the action of nitrous acid on amido compounds and their salts must be regarded as the result of two successive reactions: firstly, the formation of a diazo-body, like  $C_6H_5.N:N.OH$  or its salt; and, secondly, the action of this body on the amine with liberation of water.

Thus, the diazo-amido compounds are obtained with the chlorides of the diazo compounds by the action of  $NaNO_2$  on  $R.NH_2.HCl$  in neutral solution; but in an alkaline solution there is formed only the diazo-amido compound. For example,

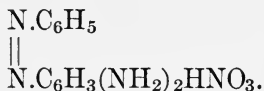


The diazo-amido compounds are also obtained by the action of  $\text{N}_2\text{O}_3$  on a cooled alcoholic solution of the amine; the diazo-amido body, being but slightly soluble, immediately separates out. The ethereal solution of the amine may also be treated with a nitrous ester.

In the preparation of the diazo-amido bodies, it is necessary to take into consideration the ease with which they pass into the isomeric amido-azo compounds.

(c) **Azo Derivatives.**—In certain cases, in the reaction of diazo-salts on amido compounds, in place of diazo-amido bodies, there are directly obtained their isomers, the amido-azo compounds.<sup>1</sup>

If meta-phenylene-diamine,  $\text{C}_6\text{H}_4 \begin{array}{l} \text{NH}_2 \\ \text{NH}_2 \end{array}$ , is added to diazo-benzene nitrate,  $\text{C}_6\text{H}_5\cdot\text{N}:\text{N}\cdot\text{ONO}_2$  (action of nitrous acid on aniline nitrate,  $\text{C}_6\text{H}_5\cdot\text{NH}_2\cdot\text{HNO}_3$ ), there is formed chrysoidine nitrate:



It is not necessary, in the preparation of these bodies, to separate the diazo-salts; they may be obtained by the action of nitrous acid on a mixture of the amines. Thus, if a cooled alkaline solution of sodium nitrite is gradually added to a mixture of the hydrochlorides of aniline and dimethylaniline, there is formed:



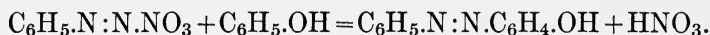
<sup>1</sup> For the formation of the azo derivatives by direct addition, see p. 155.

In the same manner, by the action of nitrous acid on meta-phenylene-diamine, triamido-azo-benzene is formed:



It is probable that there is at first formed  $\text{NH}_2.\text{C}_6\text{H}_4.\text{N}:\text{N}.\text{OH}$ , which then reacts on another molecule of  $\text{C}_6\text{H}_4(\text{NH}_2)_2$ .

The salts of the diazo compounds react readily with phenols and their derivatives:



To prepare hydroxy-azobenzene, a solution of 30 gms. of potassium nitrite in 4 litres of water is added to a solution of 20 gms. of phenol in 2 litres of water. On agitating, there is at first formed a yellow precipitate which becomes red. After standing for 24 hours, the precipitate is dissolved in ammonia in order to separate it from resinous matters. The solution is reprecipitated by the addition of acid, and the compound is finally crystallized from boiling dilute alcohol.

In the reactions of diazo-salts on phenols and amines, the  $\text{N}:\text{N}$  group takes the para-position generally with respect to the  $\text{OH}$  or  $\text{NH}_2$  group, and the ortho-position when the para is occupied.

The salts of the diazo compounds condense also with metallic derivatives, with nitro compounds of the aliphatic series, with esters, and with ketonic acids like aceto-acetic acid; but in such cases azo derivatives are not obtained, but derivatives of phenyl hydrazine. Thus, with aceto-acetic ester, there is

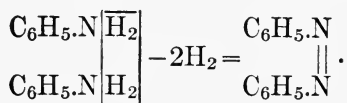
formed the ester of a rather stable acid,

$$\text{C}_6\text{H}_5.\text{N}:\text{N}=\overset{\text{H}}{\underset{\text{C}}{\text{C}}}.\overset{\text{CO}.\text{CH}_3}{\underset{\text{CO}.\text{OC}_2\text{H}_5}{\text{C}}},$$

which only decomposes at  $180^\circ \text{C}$ ., giving carbonic acid and  $\text{CH}_3.\text{CO}.\text{CH}:\text{N}.\text{NH}.\text{C}_6\text{H}_5$ .

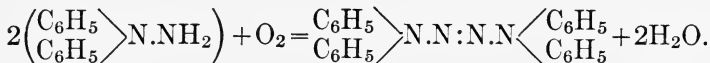
The azo compounds are obtained by the oxidation of aromatic amido compounds,  $4\text{H}$  being removed from two molecules

of the amine. Thus, aniline, oxidized with potassium permanganate, gives azo-benzene:

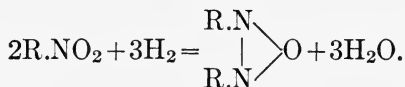


Other oxidizing agents may also be employed, such as potassium ferricyanide in alkaline solution, chromic acid in acetic acid solution, hydrogen peroxide,<sup>1</sup> or even by passing the vapors of the amine over heated lead oxide.

The oxidation of the disubstituted hydrazines may be carried out by agitating their aqueous or alcoholic solution with the oxide of mercury or silver,  $\text{Hg}_2\text{O}$ , or  $\text{Ag}_2\text{O}$ , or by employing ferric chloride. The disubstituted hydrazines are easily decomposed:



(d) **Azoxy Compounds.**—The aromatic nitro compounds, by the action of alkaline reducing agents, are converted into azoxy compounds by the removal of three molecules of oxygen from two molecules of the nitro-body:



The nitro-body is treated with an alcoholic solution of caustic potash (Zinin's process). In some cases, for example with azoxy-benzene, a better result is obtained by using sodium methylate dissolved in methyl alcohol. To prepare the azoxy bodies, it is convenient to employ sodium amalgam, which is

<sup>1</sup> Barzilovsky, *On the Azo Derivatives of Toluene*, Kieff, 1878 (in Russian).

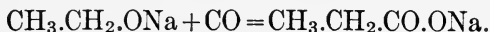
allowed to act on the aqueous or alcoholic solution of the nitro-compound. To avoid the formation of an azo-body, produced by the oxidation of the hydrazo compound which is at first formed, the sodium amalgam is added, a little at a time, and in slight excess only, at a temperature as low as possible. There is always formed a small quantity of azo derivative, which is removed by treating the product with tin chloride,  $\text{SnCl}_2$ , and sulphuric acid. Zinc dust, caustic potash, and stannous oxide in alkaline solution, are all good reducing agents, but they react too energetically; they are only employed for the preparation of hydrazo or azo bodies.

## CHAPTER VIII.

### TYPES OF SYNTHESSES.

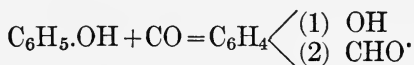
#### I. FIXATION OF CARBON MONOXIDE (CO).

CARBON monoxide combines with alkalies, and gives salts of formic acid; it also combines with alcoholates to give salts of the homologues of formic acid:



If, instead of an alcoholate, there is taken its mixture with a salt of an acid, there are obtained acids having an increased number of carbon atoms.

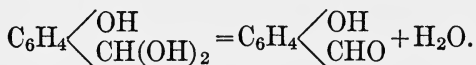
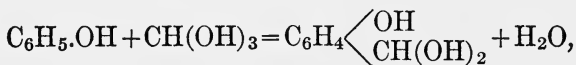
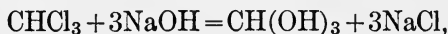
Carbon monoxide, at the moment of its formation, combines with phenols and their derivatives, the hydrogen of the CH group passing into the CHO group. Phenol, in this manner, is converted into salicyl aldehyde by the simultaneous action of caustic soda and chloroform:



In carrying out this reaction, two to three times the theoretical amounts of chloroform and caustic soda are taken; the chloroform is added drop by drop to the alkaline solution of the phenol slightly heated; by raising the temperature the reaction is finally completed. The liquid is then acidulated; the excess of phenol is distilled off in a current of steam; then the liquid is filtered to remove resinous matters, and the aldehyde which has been formed is extracted with ether. If it

distils with steam, it is separated from the phenol by means of sodium bisulphite,  $\text{NaHSO}_3$ . Distillation in steam can also be used in order to separate the isomers which may be formed; ortho-oxy-aldehydes are generally much more volatile than para-isomers.

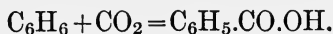
The reaction of phenols with caustic soda and chloroform can be considered as a condensation, with liberation of water, of the phenol with the tri-hydrate which is at first formed:



The formation of ketones affords a special case of the fixation of carbon monoxide; for example, the formation of ethyl-ketone,  $\text{C}_2\text{H}_5.\text{CO}.\text{C}_2\text{H}_5$ , by the action of carbon monoxide on sodium ethyl,  $\text{C}_2\text{H}_5.\text{Na}$ . Carbon monoxide, when heated with potassium, gives  $\text{K}_6\text{C}_6\text{O}_6$ , a potassium salt of hexa-oxybenzene; the same product is also obtained as a secondary product in the preparation of potassium. With alcohol this compound gives the salt of rhodizonic acid,  $\text{C}_6(\text{O}_2)(\text{O}_2)(\text{OK})_2$ .

## II. FIXATION OF CARBON DIOXIDE ( $\text{CO}_2$ ).

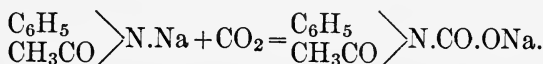
The fixation of carbon dioxide by hydrocarbons (for instance, benzene) only takes place in the presence of aluminium chloride:



With sodium compounds, however, the reaction takes place more easily. Thus,  $\text{CH}_3.\text{CH}_2\text{Na}$  gives the sodium salt of propionic acid;  $\text{NaC}\equiv\text{C}.\text{C}_6\text{H}_5$  is converted into the salt of phenyl-propionic acid.

The formation of benzoates by the action of carbon dioxide and sodium on brom-benzene,  $C_6H_5Br$ , is really the fixation of  $CO_2$  by  $C_6H_5Na$  at the moment of its formation.

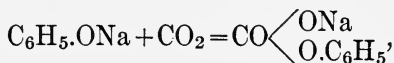
Sodium acetanilide combines with carbonic acid in the cold:



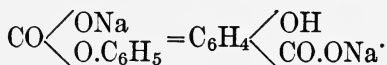
The product which is formed gives an isomer when heated, the anilide of malonic acid being formed:



The phenates combine with carbonic acid on heating, and are converted into oxy-acids; phenol gives salicylic acid. There is at first formed the salt of the acid ester of carbonic acid:



which afterwards, on heating to  $120-130^\circ C.$ , becomes isomerized into sodium salicylate:

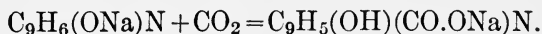


The most convenient method of preparing salicylic acid is to add liquid carbonic acid to the absolutely dry phenate enclosed in an autoclave; the mixture is heated for several hours at  $120-130^\circ C.$

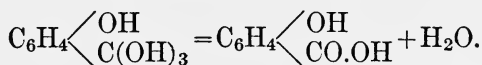
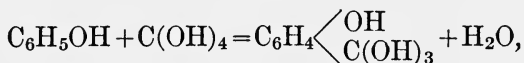
By heating sodium salicylate in a current of carbon dioxide to  $200^\circ C.$ , there are formed the salts of dicarboxyl and tricarboxylphenol acids,  $C_6H_3.OH(CO.OH)_2$  and  $C_6H_2.OH(CO.OH)_3$ . Polyhydric phenols will also combine with carbon dioxide when heated with an aqueous solution of ammonium carbonate.



The sodium compound of oxy-quinoline, heated with liquid carbon dioxide, is converted entirely into oxy-quinoline carboxylic acid:



The formation of oxy-acids by treating phenols with carbon tetrachloride,  $\text{CCl}_4$ , and caustic soda, can be considered as the fixation of carbon dioxide in the nascent state, or as a condensation of the tetrahydrate of carbon and phenol with loss of water:

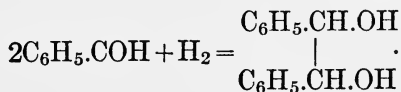


The reaction is brought about by adding carbon tetrachloride and alcohol to a strongly alkaline solution of phenol until completely dissolved; the mixture is then heated in a sealed tube until sodium chloride is no longer formed.

The fixation of carbon dioxide can be brought about by the substitution of H by CN, which is then saponified; or the  $\text{SO}_2.\text{OH}$  group may be replaced by  $\text{CO.OH}$ .

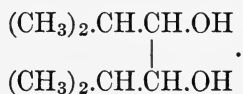
### III. CONDENSATION BY THE TRANSFORMATION OF THE CO GROUP INTO C.OH AND C.OX.

In the reduction of aldehydes and ketones, two molecules combine with the addition of hydrogen to form dihydric alcohols; and the CO group is converted into C.OH. Benzaldehyde behaves in this manner; with zinc and hydrochloric acid in alcoholic solution it gives hydrobenzoin:

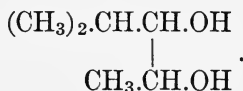


The sodium derivative of this glycol can be obtained by the action of sodium amalgam on benzaldehyde in the absence of water.

Some aldehydes of the aliphatic series are converted into dihydric alcohols by the use of alcoholic soda. Thus, isobutyric aldehyde,  $(\text{CH}_3)_2\text{CH}.\text{CHO}$ , gives a glycol simultaneously with isobutyric acid:

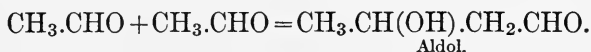


The reaction may also be carried out by the condensation of two different aldehydes. Thus, a mixture of ordinary aldehyde and isobutyric aldehyde with sodium amalgam will give:

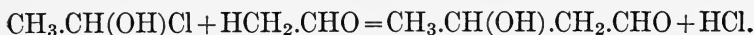
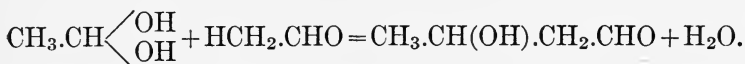


For the formation of the compound,  $[(\text{C}_6\text{H}_5)_2\text{CSH}]_2$ , see under substitutions.

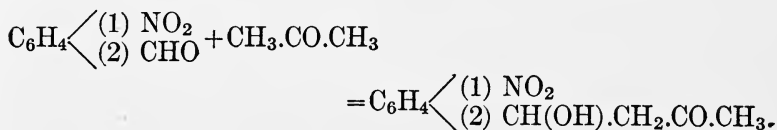
The reduction of the CO group to C.OH does not take place by the action of free hydrogen, but by the hydrogen of another molecule of the same substance. The formation of aldol according to Wurtz, by the action of hydrochloric acid on aldehyde, is a reaction of this kind:



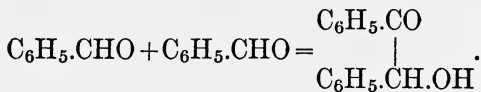
The formation of aldol may be considered as a condensation of a dihydrate with aldehyde and liberation of water, or as a condensation of chlorhydrin,  $\text{CH}_3\text{CH}(\text{OH})\text{Cl}$ , with aldehyde and liberation of hydrochloric acid:



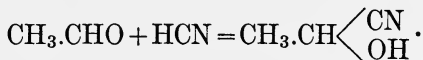
A 1 per cent. solution of caustic soda on a solution of ortho-nitrobenzaldehyde in acetone, gives rise to a reaction which may be expressed as follows:



In the aromatic series the condensation of aldehydes takes place a little differently; that is to say, the CO group of the aldehyde radical is converted into C.OH at the expense of the hydrogen of the other CHO group. It is in this manner that benzaldehyde is converted into benzoin by the action of a dilute alcoholic solution of potassium cyanide:



The conversion of the CO group into C.OH is also brought about by the union of hydrocyanic acid with aldehydes and ketones:

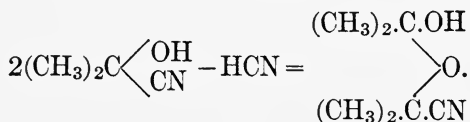


This reaction is carried out by leaving the aldehyde in contact with the theoretical quantity of hydrocyanic acid (25 per cent. aqueous solution) at the ordinary temperature, or by slightly heating. The acid reacts more readily in the nascent condition; to obtain this condition, the aldehyde or ketone in ethereal solution is mixed with the theoretical quantity of moist potassium cyanide, after which there is added drop by drop the calculated amount of a concentrated mineral acid.

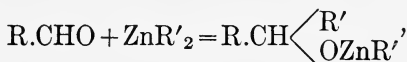
In certain cases, the cyanhydrins of dihydrates<sup>1</sup> which are

<sup>1</sup> The anhydrides of the glycols also combine with hydrocyanic acid to form cyanhydrins. Through the intervention of the cyanhydrins it is possible to replace the CO group of aldehydes and ketones by the group  $\text{C} \begin{array}{l} \swarrow \text{OH} \\ \searrow \text{CO.OH} \end{array}$ .

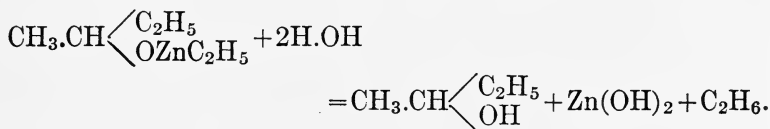
formed (as, for example, acetone cyanhydrin) readily condense with splitting-off of hydrocyanic acid:



A series of synthetic methods is based on the transformation of the CO group into C.OX, brought about by the action of metallo-organic compounds on aldehydes, ketones, etc. The aldehydes at first give condensation products:



which subsequently, on decomposition with water, replace the OZnR' group with OH and form secondary alcohols:



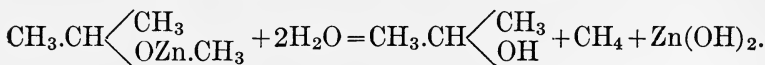
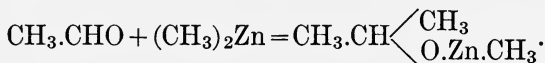
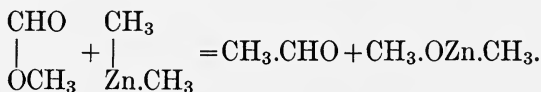
Formaldehyde, with organic compounds of zinc, gives primary alcohols.

The reaction takes place well only with zinc-ethyl or zinc-methyl; with the higher homologues, ZnR<sub>2</sub>, there occurs at the same time a reduction of the aldehyde to the corresponding alcohol.

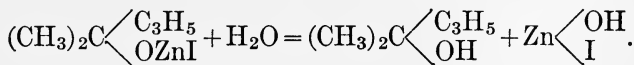
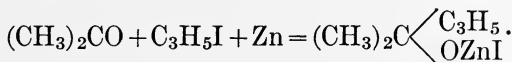
The halogen substituted compounds of the aldehydes only react well with zinc-ethyl; with the homologues of the latter, there is simply a reduction of the aldehyde.

The general method of obtaining secondary alcohols (Wagner's method) is by the action of water on the condensation products of aldehydes with organo-metallic compounds.

The action of formic and acetic esters on organo-metallic compounds can be considered in two phases: there is at first formed aldehyde, which then reacts with another molecule of the organo-metallic compound. Thus, the preparation of isopropyl alcohol, according to the general method of Zaytzeff for the making of secondary alcohols, can be expressed by the following equations, which represent the action of ethyl formate on zinc-methyl:



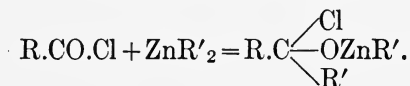
The ketones behave in exactly the same manner as aldehydes, not only with organo-metallic compounds, but also with Zn and RI; condensation products are obtained which are decomposed with water with formation of tertiary alcohols. This is a general method applied by Zaytzeff for the preparation of unsaturated tertiary alcohols.<sup>1</sup> Thus acetone, by treatment with zinc and allyl iodide, followed by water, gives allyl-dimethyl-carbinol:



The preparation of tertiary alcohols by Butleroff's method (action of organo-metallic compounds on acid chlorides) can be considered as the result of a reaction between the organo-

<sup>1</sup> With the exception of ketones containing the CH<sub>3</sub> group, as these form condensation products.

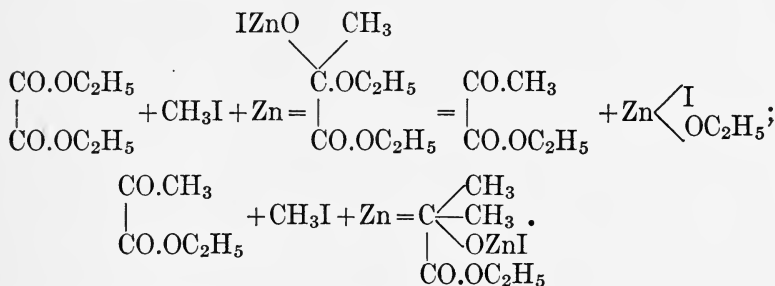
metallic compound and a ketone at first formed; but it is more probable that it is simply a replacement of chlorine by R in the condensation product formed in the first place:<sup>1</sup>



To prepare the tertiary alcohols by allowing  $R.CO.Cl$  to act on  $ZnR'_2$ , it is necessary to cool the compound which is at first formed before decomposing it with water; otherwise but a very small yield of alcohol will be obtained. The reaction with  $ZnR_2$  proceeds slowly, and, if the product of the reaction is immediately decomposed with water, only a ketone will be obtained.

With zinc-propyl and acetyl-chloride,  $CH_3.CO.Cl$ , the product which is formed,  $CH_3.C \begin{array}{l} \swarrow C_3H_7 \\ \searrow OZnC_3H_7 \\ \nearrow Cl \end{array}$ , is decomposed by

water with the formation of a secondary alcohol. The preparation of oxy-carboxylic acids, by the action of  $RI$  and zinc on oxalic ester, can be considered as a transformation of the  $CO$  group. For example, the preparation of dimethyl-glyoxalic acid may be represented as follows:



The zinc derivative, by the action of water, splits off  $OZnI$  for  $OH$ .

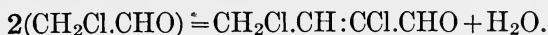
<sup>1</sup> P. Menchtchikoff, *On the Reaction of Zinc Ethyl on Butyrene*, Kazan, 1887 (in Russian).

## IV. CONDENSATION WITH LOSS OF WATER.

It is probable that, in the majority of cases, the liberation of water is only a second phase of condensations, and the compound at first formed is after the type of an aldol. In fact, if ordinary aldehyde is heated to 100° C. with dehydrating agents, such as a concentrated solution of sodium acetate, the aldol, which is at first formed by the loss of water, is converted into crotonic aldehyde,  $\text{CH}_3\text{CH}:\text{CH}\cdot\text{CHO}$ . C $\alpha$ nanthol behaves in the same manner on treatment with alcoholic potash or a small quantity of zinc chloride.

Acetic acid condenses with benzaldehyde to give cinnamic acid,  $\text{C}_6\text{H}_5\text{CH}:\text{CH}\cdot\text{CO}\cdot\text{OH}$ ; it may be assumed that this acid is derived from phenyl-lactic acid,  $\text{C}_6\text{H}_5\text{CH}_2\text{CH}(\text{OH})\cdot\text{CO}\cdot\text{OH}$ , otherwise known as tropic acid.<sup>1</sup>

In certain cases, the condensation takes place readily, even without dehydrating agents. Thus, chlor-aldehyde, heated alone, condenses to  $\alpha$ - $\gamma$ -dichlor-crotonic aldehyde:



Two different aldehydes can condense in the same manner. With ordinary aldehyde and benzaldehyde, there is formed the aldehyde,  $\text{C}_6\text{H}_5\text{CH}:\text{CH}\cdot\text{CHO}$ . This reaction is carried out by saturating the mixed aldehydes with hydrochloric acid gas and heating, or even by leaving the mixed aldehydes for 8 to 10 hours at 30° C. with a dilute solution of caustic soda.

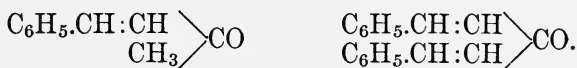
It is probable that in these condensations the CO group of one molecule always reacts with that carbon group attached to the CO group in the other molecule.

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<sup>1</sup> With Perkin's reaction it is possible to prepare an acetyl derivative of phenyl-acetic acid,  $\text{C}_6\text{H}_5\text{CH}(\text{C}_2\text{H}_3\text{O})\text{CH}_2\text{COOH}$ ; but this compound decomposes at the temperature at which the reaction takes place into acetic and cinnamic acids. An acetyl derivative is apparently obtained by heating benzaldehyde with an iso-butyrate and acetic anhydride. This compound,  $\text{C}_6\text{H}_5\text{CH}(\text{C}_2\text{H}_3\text{O})\cdot(\text{CH}_3)_2\text{COOH}$  is not decomposed with the formation of acetic acid.

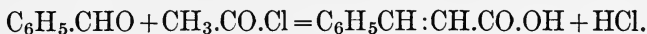
Ketones condense in the same manner as aldehydes. Acetone gives mesityl oxide, phorone, and mesitylene. There is also formed between the acetone and mesityl oxide an intermediate compound analogous to aldol:  $(\text{CH}_3)_2\text{C}(\text{OH})\cdot\text{CH}_2\cdot\text{CO}\cdot\text{CH}_3$ . This, with concentrated sulphuric acid, is decomposed into water and mesityl oxide:  $(\text{CH}_3)_2\text{C}:\text{CH}\cdot\text{CO}\cdot\text{CH}_3$ .

In condensations between ketones and aldehydes (but only those of the aromatic series), the oxygen of the aldehyde is eliminated in the form of water. Acetone and benzaldehyde, for instance, give benzylidene acetone; then another molecule of aldehyde reacts to form dibenzylidene acetone:



The ketophenone, containing but one  $\text{CH}_3$  group, only reacts with one molecule of benzaldehyde to form  $\text{C}_6\text{H}_5\cdot\text{CH}:\text{CH}\cdot\text{CO}\cdot\text{C}_6\text{H}_5$ . The condensation takes place in a closed vessel; the mixture, well cooled and saturated with hydrochloric acid gas (or the alcoholic or aqueous solution of the substances to be condensed, with the addition of a little caustic soda), is allowed to stand for some days; it is then extracted with ether.

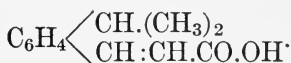
The synthesis of unsaturated acids is carried out by the reaction of Bertagnini and by that of Perkin, which is a modification of the former. Bertagnini has succeeded in synthesizing cinnamic (phenyl-acrylic) acid by heating benzaldehyde with acetyl chloride:



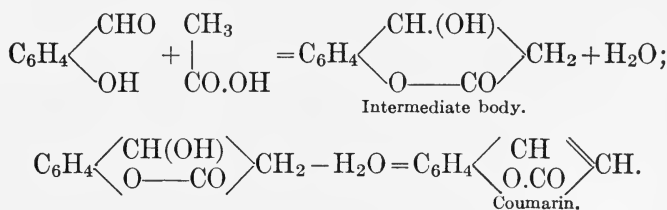
Perkin has effected the same synthesis by an analogous procedure, which he has applied to the preparation of a number of unsaturated acids. He allows the aldehyde to react on the acid in the presence of dehydrating agents, taking generally the sodium salt of the acid and using acetic anhydride as the condensing agent, or, which is better still, the anhydride of the



acid used. This reaction takes place with aldehydes of both the aliphatic and aromatic series and their derivatives. Thus, cuminic aldehyde, with sodium acetate, gives cuminyly-acrylic acid:

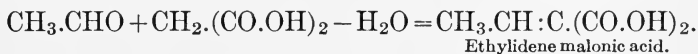


The phenol aldehydes, like salicyl-aldehyde, give unsaturated oxy-acids or their lactones. Thus, salicyl-aldehyde with acetic acid gives coumarin, the lactone of coumaric acid. In this reaction, according to Grimaux, there is formed an intermediate body of the aldol type, which loses the elements of water at the moment of its formation:



This reaction is carried out by heating 1 part aldehyde, 1 part dehydrated sodium acetate, and  $1\frac{1}{2}$  parts acetic anhydride for 8 to 12 hours on an oil-bath at  $150\text{--}160^\circ\text{C}$ ., using an inverted condenser. The product of the reaction is dissolved in a dilute alkaline solution; the unattacked aldehyde is removed by ether. The coumarin is precipitated from its alkaline solution by addition of hydrochloric acid, and is crystallized from benzene.

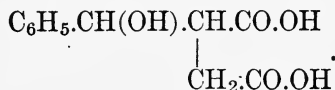
Aldehydes and ketones also condense with dicarboxylic acids. Thus:



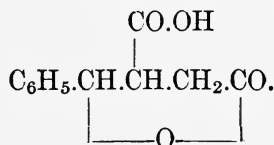
The reaction is carried out by saturating the cooled mixture of aldehyde and acid with hydrochloric acid gas, or by heating the mixture in a sealed tube with acetic anhydride or glacial acetic acid. Secondary products are obtained; in the above example,

for instance, some crotonic acid is formed by reason of the splitting-off of carbon dioxide.

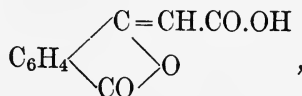
Succinic acid, in condensing, also gives rise to intermediate compounds of the aldol type, but only in the form of the sodium salt. With benzaldehyde, the salt of the following oxy-acid is formed:



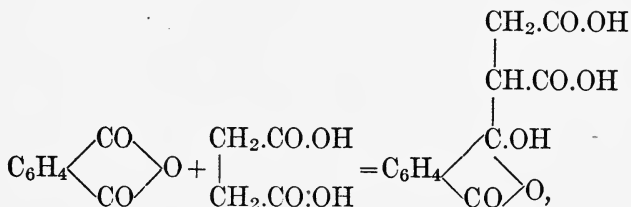
This acid, on treatment with acetic acid, immediately decomposes with the formation of a lactone:



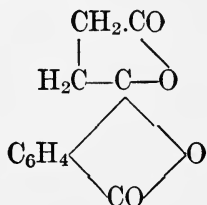
The anhydrides of the dicarboxylic acids (for example, phthalic anhydride) behave in the same manner as aldehydes. Heated with sodium acetate and acetic anhydride, it gives phthalyl-acetic acid, which does not have a symmetrical formula as usually believed; it may be represented by



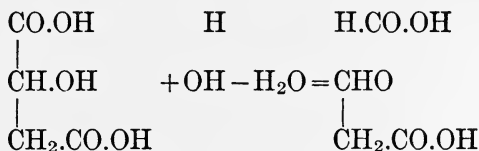
which, in fact, is a phthalide derivative. The compound obtained by the action of phthalic anhydride on succinic acid,



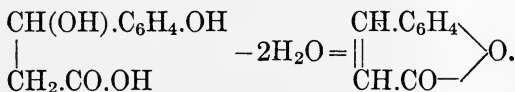
is immediately decomposed with loss of water and carbon dioxide to form a double lactone:



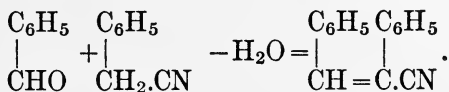
There also exist other synthetic methods, in which the formation of compounds belonging to the aldol type play an important rôle. The preparation of coumarin, by heating phenol with malic acid, can be explained by admitting the formation of the aldehyde of malonic acid with liberation of formic acid:



this aldehyde immediately combines with phenol, and the product so formed is decomposed into water and coumarin:

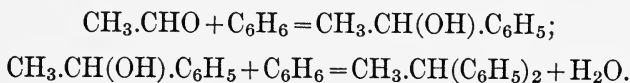


Benzaldehyde also condenses with benzyl cyanide in the presence of sodium alcoholate:



It is not impossible, in the synthesis of hydrocarbons, by the aid of dehydrating agents, to obtain aromatic aldehydes

and hydrocarbons with formation of compounds of the aldol type, which further react to give more complicated bodies. The formation of diphenyl-ethane, for example, from aldehyde and benzene may be expressed by the following equations:

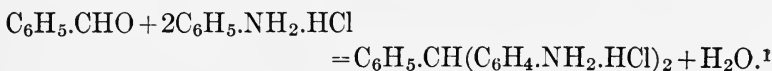


A solution of aldehyde is heated with a large quantity of concentrated sulphuric acid, and the theoretical quantity of benzene is added; then, after some hours' standing, the hydrocarbon is removed with water. It is better to use the acetals than the aldehydes themselves.

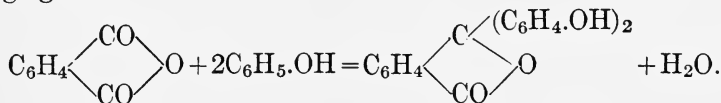
Aldehydes also condense with different derivatives of aromatic hydrocarbons. Thus, if a well-cooled mixture of aldehyde and phenol is added drop by drop to tin chloride, the following reaction takes place:



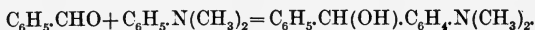
Benzaldehyde, heated with aniline hydrochloride in the presence of zinc chloride, condenses as follows:



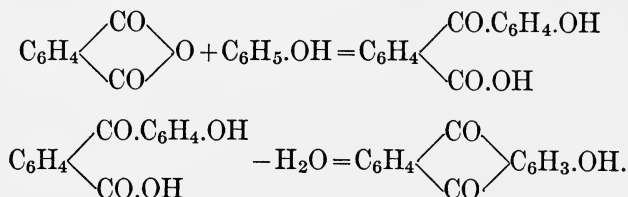
Phthalic anhydride condenses with phenols in the same manner as aldehydes and ketones in the presence of dehydrating agents:



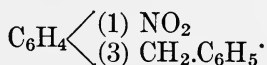
<sup>1</sup> The hypothesis that compounds of the aldol type are at first obtained is confirmed by the fact that benzaldehyde with dimethylaniline, in the presence of a mineral acid, reacts according to the following equation, giving a derivative of benzhydryl:



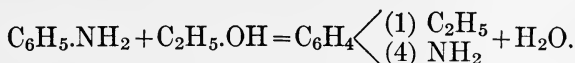
The reaction, however, may be different; thus, if phenol is added to a heated mixture of phthalic anhydride and sulphuric acid, hydroxy-benzoyl-benzoic acid<sup>1</sup> is formed, which then, by loss of water, forms hydroxy-anthraquinone:



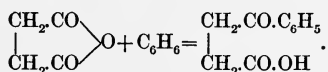
The aromatic compounds also condense (with loss of water) with different alcohols of the aliphatic and aromatic series. Benzene with benzhydrol gives triphenylmethane.<sup>2</sup> The reaction only takes place in the presence of dehydrating agents. Usually, a mixture of the reacting bodies with  $\text{P}_2\text{O}_5$ ,  $\text{ZnCl}_2$ , or  $\text{H}_2\text{SO}_4$ , is heated. Thus, nitro-benzyl alcohol condenses with benzene by simply shaking with concentrated sulphuric acid, to give:



In the same manner, by heating to  $250\text{--}300^\circ \text{C.}$ , a mixture of aniline (and its homologues, or their salts) with ordinary alcohol (or its homologues) in the presence of zinc chloride or phosphoric anhydride, there is a condensation with loss of water:



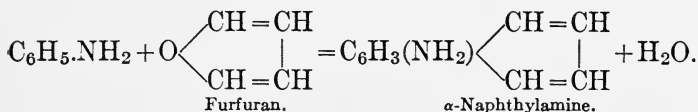
<sup>1</sup> A similar reaction occurs in the action of anhydrides in the presence of aluminium chloride. If a small amount of aluminium chloride is added to a hot solution of succinic anhydride in benzene, there is obtained:



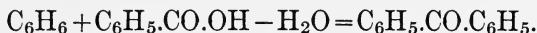
<sup>2</sup> Hemilian, *On Some Homologues and Isomerides of Triphenylmethane*, St. Petersburg, 1886 (in Russian).

As a secondary product, there is sometimes obtained a secondary base.

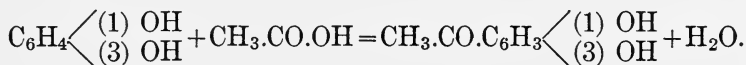
It is interesting to note the formation of  $\alpha$ -naphthylamine (from the condensation of aniline with furfuran) by heating pyromucic acid, aniline, and zinc chloride:



Aromatic compounds also condense with various acids. By heating acids or their anhydrides with hydrocarbons in a sealed tube, together with phosphoric anhydride, ketones are produced:



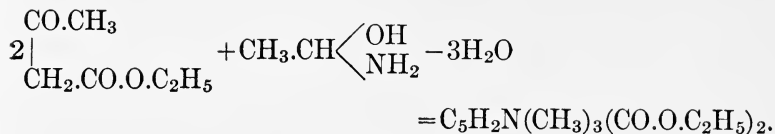
Phenols react more easily than hydrocarbons; dioxy-acetophenone is obtained by heating to  $150^\circ\text{C}$ . glacial acetic acid with resorcin and zinc chloride:



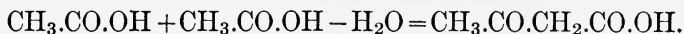
By heating aniline with acetic anhydride and zinc chloride, the acetyl group enters the benzene nucleus and also the  $\text{NH}_2$  group, and there is formed the compound,  $\text{CH}_3\cdot\text{CO}\cdot\text{C}_6\text{H}_4\cdot\text{NH}\cdot\text{CO}\cdot\text{CH}_3$ , which, on saponification with acids, gives amido-acetophenone,  $\text{CH}_3\cdot\text{CO}\cdot\text{C}_6\text{H}_4\cdot\text{NH}_2$ .

The ammonia-aldehydes,  $\text{R}\cdot\text{CH} \begin{array}{c} \text{OH} \\ \text{NH}_2 \end{array}$ , readily condense with different compounds with elimination of water. With a concentrated aqueous solution of hydrocyanic acid, they form nitriles of the  $\alpha$ -amido-carboxylic acids,  $\text{R}\cdot\text{CH} \begin{array}{c} \text{CN} \\ \text{NH}_2 \end{array}$ . With aceto-acetic ester they give hydropyridine derivatives: thus, aldehyde-ammonia with aceto-acetic ester gives the ester of hydrocollidine-dicarboxylic acid:<sup>1</sup>

<sup>1</sup> N. Liubavine, *The Pyridine Compounds*, Moscow, 1887 (in Russian).

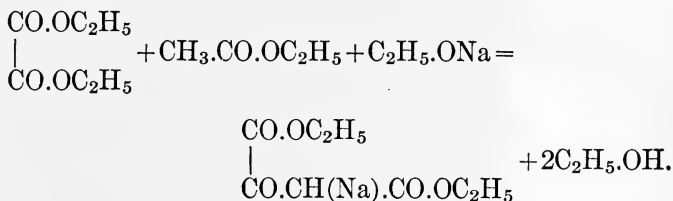


The formation of the ester of aceto-acetic acid and its analogues can also be considered as a condensation with elimination of water:

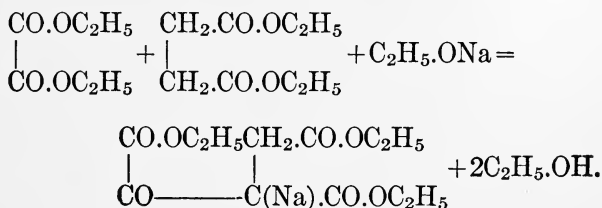


This condensation is produced, with elimination of alcohol, by the action of sodium on ethyl acetate. The other esters behave in a similar manner.

Two different acids may also be condensed; this is brought about by treating a mixture of the two esters with sodium or sodium alcoholate. For example, by using an ethereal solution of ethyl oxalate and acetate, there is obtained, by the action of sodium ethylate,  $\text{C}_2\text{H}_5.\text{ONa}$ , a sodium salt of aceto-oxalic ester:

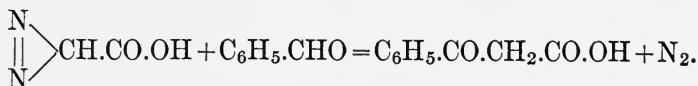


With a mixture of ethyl oxalate and succinate, there is formed an ester of succinyl-oxalic acid, a tribasic acid:



In the aromatic series, benzoyl-benzoic acid offers a case analogous to that of aceto-acetic acid. The hydroxy-benzoic acids also condense directly by the action of sulphuric acid; only, in the case of ketonic acids, there are formed closed-chain compounds, such as the hydroxy-anthraquinones.

The condensation of acids of the aromatic series with those of the aliphatic series can be brought about by means of the diazo-bodies. The ester of diazo-acetic acid, on heating with benzaldehyde and toluene, gives nitrogen,  $N_2$ , and the ester of benzoyl-acetic acid:



## V. CONDENSATION WITH LOSS OF HALOGEN ACID, OF A METALLOID, OR OF A SALT.

The halogen compounds of the aliphatic series, and those of the aromatic series containing a halogen atom in the side-chain, react with hydrocarbons, with liberation of a halogen acid:



The reaction is brought about by heating the hydrocarbon and halide with oxides of zinc, magnesium, and calcium. The aromatic hydrocarbons readily combine with halogen derivatives in the presence of zinc dust, or, better, in the presence of aluminium chloride or bromide:<sup>1</sup>



This reaction takes place with such regularity that different isomers can be obtained at will. With aluminium chloride the principal derivatives are *meta*, with zinc dust *para* and *ortho*.

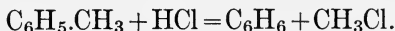
If the halogen compound is gaseous, like methyl chloride, it is passed into the heated hydrocarbon to which aluminium

<sup>1</sup> The chlorides of iron and zinc act in the same manner.



chloride has been added; if it is liquid, it is mixed with the hydrocarbon, and the metallic chloride is added little by little until the halogen acid is no longer liberated.

When the reaction is finished, the product is washed with water and then fractionated, for there is always obtained a mixture of several hydrocarbons. Thus, benzene, treated with methyl chloride besides methyl-benzene,  $C_6H_5.CH_3$ , also gives a whole series of methyl-benzenes up to the hexa compound,  $C_6(CH_3)_6$ , inclusively. This process is never complete, as by the action of the aluminium chloride a reverse reaction can take place:



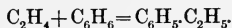
Zinc chloride acts much more slowly than aluminium chloride; nevertheless, in certain cases, it is preferable (for example, with naphthalene and benzyl chloride,  $C_6H_5.CH_2.Cl$ ), for then less secondary products are obtained. Metallic zinc only reacts by being converted into zinc chloride at the expense of the chlorine compound.

In place of chlorine derivatives, the bromine or iodine compounds may also be used. With the latter it is necessary to heat in a sealed tube with a small quantity of iodine.

Normal propyl bromide,  $CH_3.CH_2.CH_2.Br$ , on condensing with benzene under the influence of aluminium bromide, gives isopropyl-benzene,  $(CH_3)_2.CH.C_6H_5$ , for by the action of aluminium bromide alone this same bromide is converted into isopropyl bromide. Allyl chloride,  $CH_2:CH.CH_2.Cl$ , with benzene and aluminium chloride, does not give allyl-benzene, but diphenylpropane  $(C_6H_5)_2.C_3H_6$ .<sup>1</sup>

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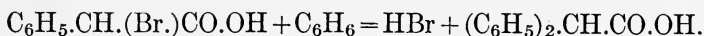
<sup>1</sup> There is consequently a substitution of chlorine by  $C_6H_5$  and a fixation of  $C_6H_6$ . An analogous case presents itself in the action of ethylene on benzene in the presence of aluminium chloride, this even being a good method for the preparation of ethyl benzene:



This reaction may be explained by admitting that the  $C_2H_4$  is first converted into  $C_2H_5Cl$ , which then reacts with  $C_6H_6$ .

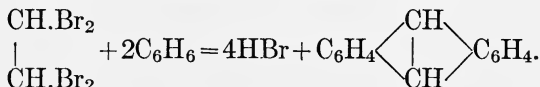
According to Friedel and Crafts, in syntheses with the aid of aluminium chlo-

Aromatic acids containing a halogen in the side-chain also condense with the aromatic hydrocarbons in the presence of the halogen salts of aluminium:



Bodies containing several halogen atoms behave in the same manner with hydrocarbons in the presence of aluminium chloride as monohalogen derivatives. Chloroform with  $\text{Al}_2\text{Cl}_6$  reacts with  $3\text{C}_6\text{H}_6$  to give triphenylmethane,  $\text{CH}(\text{C}_6\text{H}_5)_3$ . This process, in fact, is used for the preparation of the latter body; as a secondary product, diphenylmethane,  $\text{CH}_2(\text{C}_6\text{H}_5)_2$ , is formed.

With carbon tetrachloride and benzene, in the presence of aluminium chloride,  $\text{Cl}_4$  is not replaced by  $(\text{C}_6\text{H}_5)_4$ , as would at first be thought; only  $3\text{Cl}$  are replaced, and  $\text{CCl}(\text{C}_6\text{H}_5)_3$ , triphenyl-chlor-methane, is formed. Acetylene tetrabromide with benzene and aluminium chloride gives anthracene and a small quantity of triphenylethane and brom-benzene:<sup>1</sup>

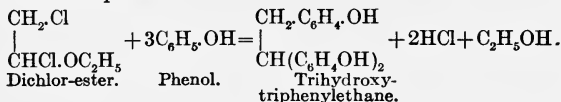


ride there is formed an organo-metallic compound (which they have not been able to isolate, however) between  $\text{Al}_2\text{Cl}_6$  and the benzene (or other hydrocarbon), with liberation of hydrochloric acid:

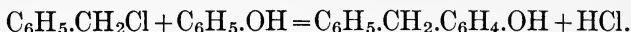


This compound then reacts with halogen derivatives, regenerating  $\text{Al}_2\text{Cl}_6$ . According to Gustavsonn, however, by the action of  $\text{Al}_2\text{Cl}_6$  on aromatic hydrocarbons, condensation products are formed, as, for example,  $\text{Al}_2\text{Cl}_6.6\text{C}_6\text{H}_6$ . During their formation there would be considerable heat liberated which would account for their strongly increased reactivity.

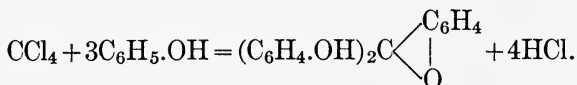
<sup>1</sup> An interesting formation of derivatives of triphenylethane is in the condensation of phenols with the dichlor-esters. If the phenol is intimately mixed with the dichlor-ester, the mixture heats up, a brisk reaction takes place, with liberation of hydrochloric acid and ethyl chloride. With an excess of phenol a reddish-colored resinous substance is obtained soluble in alkalis. The reaction may be thus expressed:



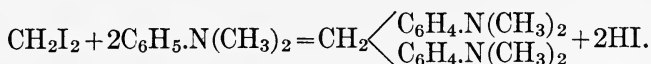
Phenols, in the presence of zinc dust or zinc chloride, react like hydrocarbons with the halogen compounds:



Phenol with carbon tetrachloride and a small quantity of zinc chloride gives aurine:

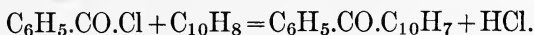


The halogen compounds condense very readily with tertiary amines:

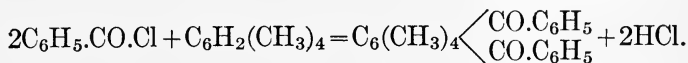


This reaction is carried out on a water-bath without any condensing agent.

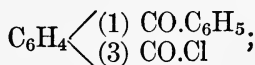
The acid chlorides of both the aliphatic and aromatic series condense with hydrocarbons (in the presence of aluminium and zinc chlorides) to form ketones:



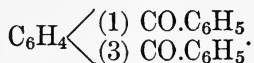
Two molecules of the acid chloride and one molecule of the hydrocarbon may also take part in the reaction:



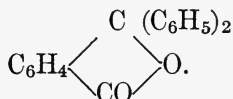
Chlorides of dicarboxylic acids react with either one or two molecules of the hydrocarbon; thus, the chloride of isophthalic acid with one molecule of benzene gives:



while with two it gives isophthalophenone:

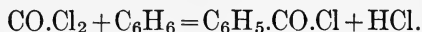


Phthalyl chloride with benzene, in the presence of aluminium chloride, gives phthalophenone:



The preparation of the above ketones is carried out by gradually adding aluminium chloride to a mixture of the acid chloride and the hydrocarbon until there is no further liberation of hydrochloric acid.

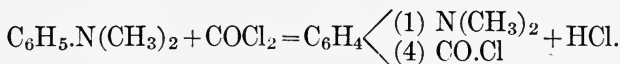
Carbonyl chloride, in the presence of aluminium chloride, reacts with hydrocarbons in the same manner as the acid chlorides. With benzene it gives benzoyl chloride:



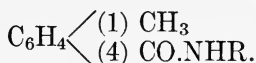
But, as benzoyl chloride reacts in turn on benzene, the final product is benzophenone:



Dimethyl-aniline, at 50° C., reacts with carbonyl chloride to give dimethyl-amido-benzoic acid, or, rather, its chloride:



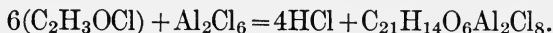
The chlorine derivatives of the substituted carbamic acids,  $\text{Cl.CO.NHR}$ , with the aromatic hydrocarbons, (for example, toluene,  $\text{C}_6\text{H}_5.\text{CH}_3$ ) give the substituted amides of the aromatic acids:



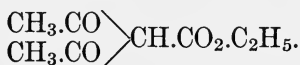
This is one of the methods of synthesizing the aromatic acids.

Cyanogen chloride, in the presence of aluminium chloride, reacts with benzene to give benzo-nitrile,  $C_6H_5.CN$ .

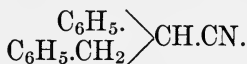
The reaction of the aliphatic acid chlorides with aluminium chloride is of interest.<sup>1</sup> Thus, acetyl chloride, diluted with chloroform, reacts with aluminium chloride at 40–45° C., liberating a large amount of hydrochloric acid gas, and forming a white crystalline substance having a composition of  $C_{12}H_{14}O_6Al_2Cl_8$ , the formation of which may be expressed by the equation:



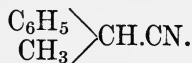
This organo-metallic compound is decomposed with alcohol into diaceto-acetic acid ester:



Benzyl cyanide,  $C_6H_5.CH_2.CN$ , easily replaces the hydrogen in the  $CH_2$  group in the presence of halogen compounds. Thus, by the action of benzyl chloride,  $C_6H_5.CH_2Cl$ , and sodium alcoholate, with benzyl cyanide, there is obtained the compound:



By gently heating a mixture of benzyl cyanide, sodium, and methyl iodide, there is produced the nitrile of hydro-atropic acid:

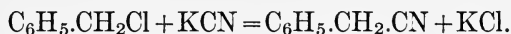


The metallic cyanides ( $KCN$ ,  $NaCN$ , ferrocyanides, etc.) react with the halogen compounds of the aliphatic series and with alkyl acid sulphates, forming nitriles. The reaction is ordinarily brought about by a prolonged boiling of the solution of halogen

<sup>1</sup> See *Jour. Soc. Phys. Chim. Russe*, vol. 20, p. 81.

compound and cyanide in dilute alcohol. The nitriles are isolated and purified by distillation; often they are not isolated, but by saponification are converted directly into carboxylic acids. The tertiary halogen compounds react with difficulty with the alkaline cyanides; the latter are replaced by the double cyanide of mercury and potassium,  $\text{Hg}(\text{CN})_2 \cdot 2\text{KCN}$ .

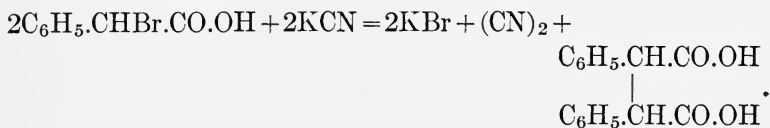
Aromatic compounds containing a halogen in the side-chain also react with metallic cyanides:



If dilute alcohol is used as a solvent, the amide of phenylacetic acid,  $\text{C}_6\text{H}_5 \cdot \text{CH}_2 \cdot \text{CO} \cdot \text{NH}_2$  is obtained as a secondary product. To convert the chloride of triphenyl-carbinol,  $(\text{C}_6\text{H}_5)_3 \cdot \text{CCl}$ , into the nitrile, it is heated with mercury cyanide,  $\text{Hg}(\text{CN})_2$ , to 150–170° C.

Halogens in the aromatic nucleus are replaced by CN only with difficulty, and never completely, even at 300–400° C.; by using potassium ferrocyanide, the reaction takes place very incompletely. The iodine compounds react somewhat more readily than the other halogen derivatives.

Brom-benzyl bromide,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{(1)} & \text{Br} \\ \text{(4)} & \text{CH}_2\text{Br} \end{smallmatrix}$ , on boiling with potassium cyanide, is converted into brom-benzyl cyanide,  $\text{C}_6\text{H}_4 \begin{smallmatrix} \text{(1)} & \text{Br} \\ \text{(4)} & \text{CH}_2\text{CN} \end{smallmatrix}$ . Phenyl-brom-acetic acid, on boiling with potassium cyanide, loses its bromine and is converted into diphenyl-succinic acid:



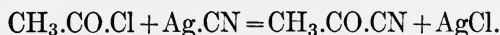
In the aromatic series, the nitriles are generally obtained through the intervention of the sulphonic acid derivatives by heating the latter with pure potassium cyanide, or with potas-

sium ferrocyanide. If necessary, the reaction may be carried out in an atmosphere of carbon dioxide. The nitrile is isolated by distillation:

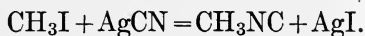


These bodies may also be obtained by replacing  $\text{NH}_2$  with  $\text{CN}$  with the aid of the azo compounds. Benzonitrile, for example, is obtained by slowly adding with agitation the solution of the diazo chloride, heated to  $90^\circ \text{C}$ ., to the double cyanide of copper and potassium. This double cyanide is prepared by adding 25 gms. of a 96 per cent. solution of potassium cyanide to a boiling solution of 25 gms. of copper sulphate in 150 cc. of water.

The acid chlorides and bromides also react, on heating, with metallic cyanides:<sup>1</sup>



Although the alkaline cyanides, potassium ferrocyanide, and the double cyanide of mercury and potassium, and some others, with the halogen compounds, give principally nitriles, other cyanides, such as those of silver and zinc and other analogous ones, form principally isonitriles or carbylamines. The reaction is carried out at  $100^\circ \text{C}$ .:

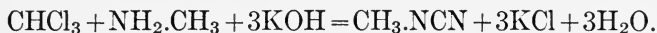


To obtain the carbylamines, for each molecule of iodide there are taken two molecules of silver cyanide, one of which serves for the formation of a double compound with the isonitrile, which is subsequently decomposed with water and potassium cyanide. The carbylamine is purified by distillation.

<sup>1</sup> For the preparation of the nitriles, see page 117; for the substitution of  $\text{OH}$  by  $\text{CN}$ , see page 198; for the combination with  $\text{HCN}$ , see page 187; and for the action of  $\text{CNCl}$ , see page 205.

With isopropyl iodide,  $(\text{CH}_3)_2\text{CHI}$ , and silver cyanide, besides the carbylamine,  $(\text{CH}_3)_2\text{CH.NC}$ , there are also formed, as secondary products, propylene and hydrocyanic acid.

The carbylamines are easily obtained by the energetic reaction of alcoholic potash on a mixture of chloroform and a salt of an amine<sup>1</sup>:



It is on this formation of carbylamine that is based the characteristic reaction for chloroform.

Compounds which contain the groups,  $\text{CO.CH}_2.\text{CO}$  or  $\text{CO.CHR.CO}$ , can have the hydrogen of these groups easily replaced by sodium, and these sodium derivatives which are formed exchange the metal for an R group by the action of the halogen compound of the aliphatic series, and, in certain cases, of the aromatic series. Aceto-acetic ester, malonic ester, and others can have one or two atoms of hydrogen replaced by a radical.

The manner of procedure is the following: A calculated quantity of sodium in the least possible amount of absolute alcohol is added to the ester, and afterwards, with cooling if necessary, the theoretical quantity of the halogen compound; finally, the reaction is finished, if required, by heating in a flask with a return condenser until the liquor is no longer alkaline. The alcohol is distilled off, and the product is washed with water to remove any halogen salt, and the ester is finally purified by distillation. If an acid chloride is allowed to act on the sodium compound, it is necessary to operate in an ethereal solution. For the preparation of diaceto-acetic ester, as much sodium as possible is dissolved, and there is added little by little an ethereal solution of acetyl chloride, taking a quantity corresponding to the sodium dissolved.

To obtain compounds containing two radicals, it is not

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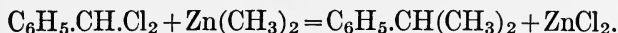
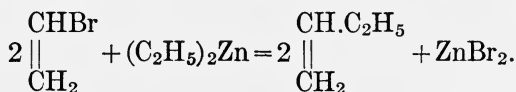
<sup>1</sup> Alexeyeff gives the formula of the isonitrile as  $\begin{array}{c} \text{CH} \\ | \\ \text{CH}_2 \end{array} \begin{array}{l} \nearrow \\ \searrow \end{array} \text{N}.$



always necessary to isolate the first body containing a single radical. After adding for each molecule of alcoholate a calculated amount of the halogen compound, and when it is no longer alkaline, a second molecule of alcoholate may be added, followed by the addition of the halogen body. This reaction is of great importance in syntheses, and is applied in a large number of cases.

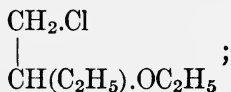
Diketones which contain  $\text{CO}.\text{CH}_2.\text{CO}$ , and compounds which have  $\text{SO}_2.\text{CH}_2.\text{CO}$ , behave like aceto-acetic ester towards the alcoholates and the halogen compounds.

Condensation, with the production of metallic halogen derivatives, takes place by the action of the organo-metallic compounds on halogen compounds:



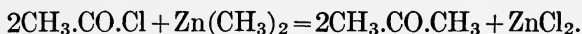
The reaction is so energetic that it is necessary to moderate it by dilution with ether, benzene, etc.

Dichlor-ethyl-ether with zinc-ethyl only replaces one atom of chlorine and forms:



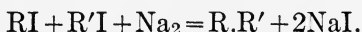
to replace the second, it is necessary to heat in a sealed tube.

The acid chlorides react very readily with the organo-metallic compounds to form ketones, a result obtained by the further action of the acid chloride on the first product of the direct action. The reaction may be expressed by the following equation:



It is necessary, after the reaction is finished, to treat the product with water or a dilute acid, especially when there is an excess of  $\text{ZnR}_2$ ; otherwise it would form tertiary alcohols. When the substances are mixed together, they should be cooled.

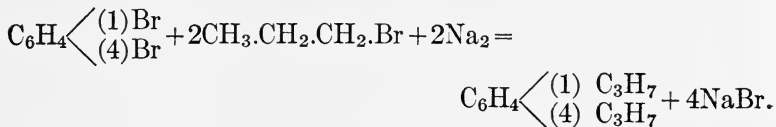
The iodine compounds, when treated with sodium, nearly all behave according to the following equation:



Usually the reaction takes place less readily with chlorine and bromine compounds.

In certain cases, by employing a mixture of halogen compounds, the reaction takes place separately on each one; this is particularly true when the bodies are not attacked with the same energy. Thus, on heating a mixture of octyl bromide and ethyl iodide with sodium, the latter is converted entirely into butane before the temperature becomes sufficiently elevated to attack the octyl bromide; also the latter is converted entirely into  $\text{C}_8\text{H}_{17}.\text{C}_8\text{H}_{17}$ .

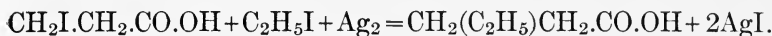
Bodies containing several halogen atoms behave in the same manner as those which only contain one:



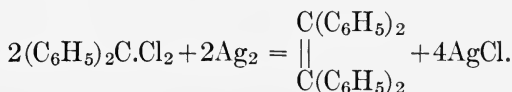
In general, the sodium is allowed to act on the mixture of the well-dried halogen compounds, and without alcohol. The mixture is cooled, if necessary, or, on the other hand, heated under a certain pressure. With secondary iodides there may be formed unsaturated hydrocarbons, but it is easy to separate these by shaking with sulphuric acid.

In the aliphatic series, the synthesis of the carboxylic acids and their esters is carried out in the same manner. Sometimes the sodium is replaced with silver obtained by the action of zinc

on silver chloride. Valerianic acid is obtained in this manner by heating  $\beta$ -iodo-propionic acid and ethyl iodide with silver at 150–180° C.:



$\beta$ -Iodo-propionic acid alone with silver gives adipic acid. With silver and  $(\text{C}_6\text{H}_5)_2\text{CCl}_2$ , we have the reaction:



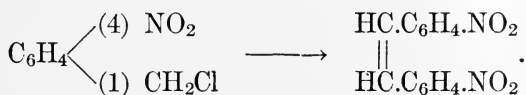
The silver may be replaced by other metals. Thus the reaction,



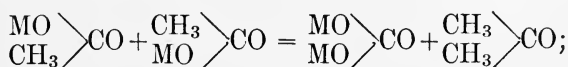
occurs on heating with copper at 200° C. Brombenzene reacts with ethyl chlor-formate,  $\text{ClCO}.\text{OC}_2\text{H}_5$ , on heating with sodium amalgam of 1 per cent.

Condensations with removal of halogen may also take place with the aid of alkaline cyanides (see page 206).

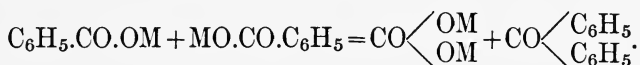
Condensation with elimination of a halogen acid takes place in certain cases through the action of an alcoholic solution of sodium. Thus, para-nitro-benzyl chloride gives dinitro-stilbene:



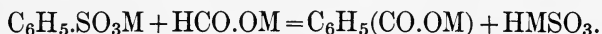
As an example of a condensation with elimination of a salt, may be given the formation of ketones by the distillation of certain salts; thus, ordinary acetone is obtained according to the following equation:



and benzophenone, in the same way, may be prepared from benzoates:

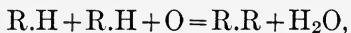


The synthesis of the aromatic carboxylic acids, by the fusion of a mixture of an aromatic sulphonic acid and a formate, is also a condensation with elimination of a salt:



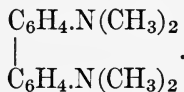
## VI. CONDENSATION WITH LIBERATION OF HYDROGEN.

The reaction expressed by the general equation,

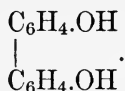


often occurs in the aromatic series. Benzene, for example, among other products, gives diphenyl when its vapors are passed through an iron tube heated to redness and filled with pumice-stone. The formation of diphenyl will explain the production of a certain quantity of benzoic acid in the oxidation of benzene with manganese dioxide and sulphuric acid. Naphthalene, by the same reaction as above, gives  $\text{C}_{10}\text{H}_7.\text{C}_{10}\text{H}_7$ .

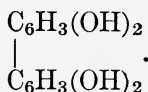
Dimethyl-aniline, dissolved in sulphuric acid and oxidized with lead oxide, is converted into tetramethyl-benzidine:



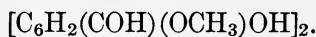
Phenol, on oxidation with potassium permanganate, gives symmetrical diphenol:



Resorcin and hydroquinone, fused with alkalies, are converted into:

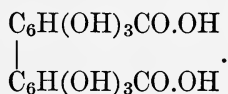


The other phenols, oxy-aldehydes, and oxy-acids of the aromatic series behave in a similar manner. Vanillin, with a hot solution of ferric chloride, gives divanillin:<sup>1</sup>

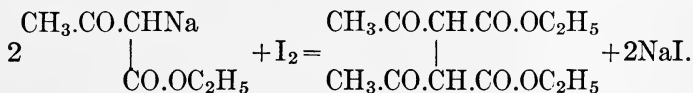


An aqueous solution of vanillin gives a bluish-violet coloration with ferric chloride; if heated, the divanillin is deposited in the form of a white crystalline substance, difficultly soluble in the ordinary solvents, but readily so in alkalies.

Gallic acid, oxidized with silver oxide or arsenic acid, gives the acid:



In certain cases, hydrogen may be removed indirectly. Thus, iodine, acting on the sodium compound of bodies containing the group,  $\text{CO.CH}_2\text{CO}$ , splits off sodium, and there is formed a condensation:



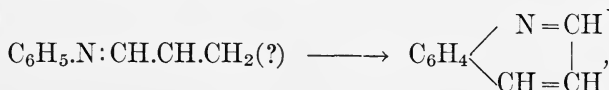
This reaction takes place by dissolving the sodium compound in ether and adding the theoretical quantity of a concentrated solution of iodine in ether.

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A Dianine, *Conversion of Phenols into Diphenols by Oxidation*, St. Petersburg, 1880 (in Russian).

## VII. CONDENSATION WITH LIBERATION OF WATER AND HYDROGEN.

This reaction takes place in the important synthesis of Skraup,—the formation of quinoline and its derivatives by heating various amido compounds with glycerol and sulphuric acid.<sup>1</sup> Quinoline is obtained in the dry distillation of the condensation product of acrolein with aniline:

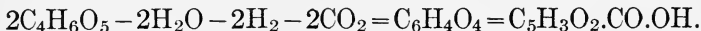


and it is known that sulphuric acid acting on glycerol will give acrolein. In the reaction of Skraup, the removal of hydrogen can be admitted in the product of condensation (with loss of water) of acrolein with amido compounds. The hydrogen which is so liberated may act as a reducing agent; hence there is added to the mixture an oxidizing agent such as nitrobenzene, or, better, sodium nitrophenate. The general method of obtaining the quinolines consists in heating for several hours, with a reflux condenser, the amido compounds with glycerol and sulphuric acid, with some nitrobenzene. The latter is removed by distillation in steam; the remaining liquor is made alkaline, and the free base is removed either by distillation in steam or by ether. Nearly all aromatic compounds give quinoline derivatives if they contain an unreplaced hydrogen in the ortho position with reference to the amido group.

## VIII. CONDENSATION WITH LIBERATION OF CO<sub>2</sub>.

The formation of ketones (see page 211) falls under this class of condensations, as well as many other cases.

Sulphuric acid acting on malic acid gives cumalic acid:



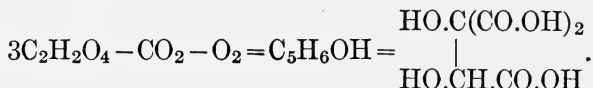
The cumalic acid may be considered as a condensation product of malonic aldehyde.

<sup>1</sup> See the Monograph of Liubavine cited on p. 198.

Tartaric acid, on dry distillation, or by the action of hydrochloric acid at 180° C., gives pyrotartaric acid:



Oxalic acid, reduced with sodium amalgam, gives desoxalic acid:



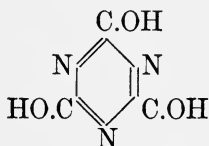
The electrolysis of aliphatic acids is effected with the liberation of carbonic acid and hydrogen with a condensation of the hydrocarbon groups which form a part of the acid radical. The electrolysis of the salts of valeric acid gives octane.

### IX. POLYMERIZATION.

Sometimes polymerization is the result of an indirect complication of the molecule; in other cases it is the result of a series of consecutive reactions; while, in others still, it is the result of direct condensation. The latter case takes place most often by the action of high temperatures on unsaturated bodies: acetylene gives benzene; valerylene and isoprene give the terpene,  $\text{C}_{10}\text{H}_{16}$ ; the terpenes themselves are converted into  $\text{C}_{20}\text{H}_{32}$ , etc. Styrol is converted into its polymeride, metastyrol.

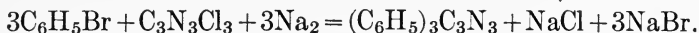
Certain bodies bring about polymerization by their simple presence. Terpenes polymerize under the influence of boron fluoride, antimony trichloride, etc.

The polymerization of cyanic acid into cyanuric acid <sup>1</sup> is the result of an indirect condensation, the nitrogen binding the groups together. The structure of cyanuric acid is:

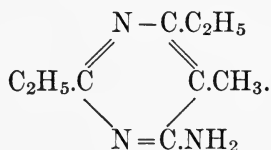


<sup>1</sup> The action of triethyl phosphine,  $\text{P}(\text{C}_2\text{H}_5)_3$ , on phenylcyanate,  $\text{CN.OC}_6\text{H}_5$ , is interesting; a minute quantity of the former is sufficient to convert a very large quantity of the latter into cyanuric ester,  $\text{C}_3\text{N}_3(\text{OC}_6\text{H}_5)_3$ .

An analogous formula is admitted for cyanphenine, the polymer of benzonitrile,  $(C_6H_5.CN)_3$ , which is formed not only by the action of sodium on benzonitrile, but also by the action of sodium on the ethereal solution of a mixture of  $C_3N_3Cl_3$  and brombenzene:



An entirely different case is presented in the polymerization of nitriles of the aliphatic series by the action of metallic sodium; there is here a direct condensation. The polymerized nitriles are found to be related to the pyrimidine derivatives,<sup>1</sup> which are obtained by the condensation of amidines with acetoacetic ester. Cyanethine, for example, very probably has the formula:



There has also been obtained a double nitrile,  $C_6H_{10}N_2$ , intermediate between propionitrile and cyanethine.

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<sup>1</sup> I. Ponomareff, *On the Constitution of Cyanuric Acid*, Odessa, 1885 (in Russian).



## CHAPTER IX.

### ISOMERIZATION.

It sometimes happens that a body is converted into an isomeric form possessing the same percentage composition, either by the same reaction which gives rise to the first body, or to some other reaction. This displacement of the atoms combined in a molecule can be explained either by the fact of successive reactions, or by the existence of a more stable form to which all the other isomers tend to transform themselves.<sup>1</sup> This latter supposition has been used in order to explain the tendency possessed by various hydrocarbons to pass into their isomers having a symmetrical structure. For example, the butylenes tend to pass into



But this fact, as well as the transformation of propyl bromide,  $\text{CH}_3.\text{CH}_2.\text{CH}_2\text{Br}$ , into isopropyl,  $(\text{CH}_3)_2\text{CHBr}$ , by the action of aluminium bromide, the formation of secondary

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<sup>1</sup> A. Eltekoff, *Molecular Transpositions among the Hydrocarbons of the Ethylene Series and among the Saturated Alcohols*, Karkoff, 1884 (in Russian). See also the theses of Gustavsonn and Ponomareff, cited on pp. 75 and 216.

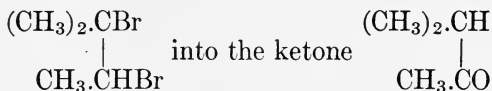
In some cases, the presence of certain groups in the molecule may be the cause of its isomerization. Vidmann and Fileti have shown the existence of certain rules in this respect. In the benzene derivatives, if the group  $\text{CH}_2.\text{CH}_2.\text{CH}_3$  is found in the para position with reference to a  $\text{CH}_3$  group, the oxidation of the latter group (conversion into  $\text{CH}_2\text{OH}$ ,  $\text{CHO}$ , or  $\text{CO.OH}$ ) is accompanied by the transposition of the  $\text{CH}_2.\text{CH}_2.\text{CH}_3$  group into  $\text{CH}(\text{CH}_3)_2$ . Inversely, the reduction of the groups  $\text{CH}_2\text{OH}$ ,  $\text{CHO}$ , or  $\text{CO.OH}$  to  $\text{CH}_3$  converts  $\text{CH}(\text{CH}_3)_2$  into  $\text{CH}_2.\text{CH}_2.\text{CH}_3$ .

butyl alcohol in place of the normal, and the tertiary in place of isobutyl alcohol, can be explained more readily by successive fixations and removals of groups.

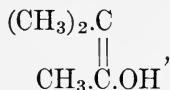
The isomerization of acetylene hydrocarbons, when they are heated with alkalis in alcoholic solution, really takes place, as shown by Favorsky,<sup>1</sup> by the fixation and then the removal of the alcoholate. Thus ethyl acetylene,  $\text{CH}_3\cdot\text{CH}_2\cdot\text{C}\equiv\text{CH}$ , heated to  $170^\circ\text{C}$ . with an alcoholic solution of caustic potash, gives dimethyl acetylene,  $\text{CH}_3\cdot\text{C}\equiv\text{C}\cdot\text{CH}_3$ . In this same manner the different cases of isomerism above noted may be explained.

Durol, or tetramethyl-benzene (symmetrical),  $\text{C}_6\text{H}_2(\text{CH}_3)_4$ , by the action of sulphuric acid, is converted into adjacent tetramethyl-benzene. There is in this case an instance of successive reactions, for at the same time there are formed sulphonic acids of the two hydrocarbons and of trimethyl-benzene, and, still further, hexamethyl-benzene. When brom-tribrom-phenol,  $\text{C}_6\text{H}_2\text{Br}_3\cdot\text{OBr}$ , is heated to  $180^\circ\text{C}$ . with concentrated sulphuric acid, it is converted into the isomer, tetrabrom-phenol,  $\text{C}_6\text{HBr}_4\cdot\text{OH}$ .

The compounds,  $\text{C}_n\text{H}_{2n}\text{Br}_2$ , heated with water and lead oxide, yield glycols or oxides at the same time as aldehydes and ketones. In certain cases this may be explained by the fixation of water to the acetylene products which are at first formed. In this manner ethylene bromide is converted into aldehyde. The conversion of the bromide of trimethyl-ethylene

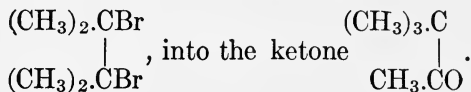


can also be explained by the fixation of water to the unsaturated alcohol,



<sup>1</sup> See *Jour. Soc. Phys. Chim. Russe*, vol. 19, pp. 414 and 553; vol. 20, p. 518.

which is at first formed, and the subsequent splitting-off of water. But the same explanation cannot be used in the case of the transformation of the bromide of di-isopropyl,



The conversion of phenyl-ethylene oxide,  $\begin{array}{c} \text{C}_6\text{H}_5.\text{CH} \\ | \\ \text{CH}_2 \end{array} \text{O}$  into phenyl-acetaldehyde,  $\text{C}_6\text{H}_5.\text{CH}_2.\text{CHO}$ , by boiling with a 20 per cent. solution, of sulphuric acid, or by the action of acetyl chloride or benzoyl chloride, is also a fixation and removal of water.

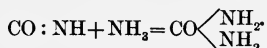
In the same manner, symmetrical diphenyl-ethylene oxide,  $\begin{array}{c} \text{C}_6\text{H}_5.\text{CH} \\ | \\ \text{C}_6\text{H}_5.\text{CH} \end{array} \text{O}$ , with dilute sulphuric acid at  $200^\circ \text{C}$ ., is converted into diphenyl-acetaldehyde,  $(\text{C}_6\text{H}_5)_2\text{CH}.\text{CHO}$ .

$\alpha$ -Benzene pinacoline,  $\begin{array}{c} (\text{C}_6\text{H}_5)_2.\text{C} \\ | \\ (\text{C}_6\text{H}_5)_2.\text{C} \end{array} \text{O}$ , is converted into the  $\beta$  compound,  $(\text{C}_6\text{H}_5)_3\text{C}.\text{CO}.\text{C}_6\text{H}_5$ , when it is heated to  $150^\circ \text{C}$ . with hydrochloric or hydrobromic acids.<sup>1</sup>

Compounds containing nitrogen often give rise to cases of isomerization. When ammonium cyanate is heated it gives urea;<sup>2</sup> the substituted ureas and the thio-ureas may be obtained

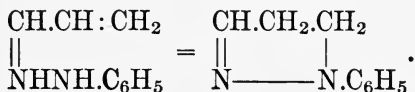
<sup>1</sup> A. Zagumenny, *On the Aromatic Pinacones and Pinacolines*, St. Petersburg, 1881 (in Russian).

<sup>2</sup> The synthesis of urea can be regarded as the dissociation of ammonium cyanate into cyanic acid,  $\text{CO}:\text{NH}$ , and ammonia, which then recombine in a different manner:

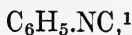


Inversely, urea, heated in a sealed tube with alcoholic potash, gives cyanic acid and ammonia.

in the same manner. The esters of true cyanic acid heated to 200–210° C. are converted into the isocyanic esters. The phenylhydrazines, on heating, give pyrazolines:



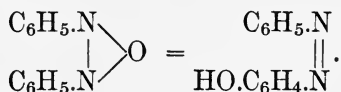
The isonitriles, on prolonged heating, are changed into nitriles. Thus,



heated to 200° C., is converted into  $\text{C}_6\text{H}_5.\text{CN}$ .

The aromatic ketoximes, by the action of various agents, yield isomeric anilides. The oxime derivative of benzophenone,  $(\text{C}_6\text{H}_5)_2\text{C:N.OH}$ , dissolved in acetic acid, by the action of gaseous hydrochloric acid at the ordinary temperatures, is converted into benzanilide,  $\text{C}_6\text{H}_5.\text{CO.NH.C}_6\text{H}_5$ .

Azoxy compounds are converted into oxy-azo derivatives by sulphuric acid:



The isomerization in this case can be considered as the result of the reaction between the hydrate of diazobenzene,  $\text{C}_6\text{H}_5\text{N:N.OH}$ , or, more exactly, its sulphate, and phenol formed by the decomposition of the azoxy-benzene by the sulphuric acid.

The diazo-amido compounds, for example,



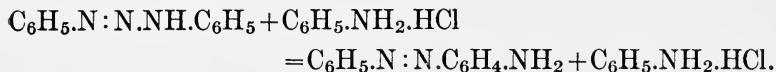

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<sup>1</sup> The formula for this body as given by Alexeyeff is  $\text{C}_6\text{H}_5 \begin{array}{c} \text{CH} \\ \diagup \quad \diagdown \\ || \\ \text{N} \end{array}$ .

are converted into amido-azo derivatives,

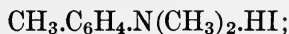


by a prolonged cooling of their solutions, but more readily by the action of aniline hydrochloride:



There is at first formed, without doubt, diazobenzene chloride,  $\text{C}_6\text{H}_5\text{N}:\text{N}.\text{Cl}$ , and aniline, which subsequently react with each other.

When the secondary aromatic amines are heated they are converted into the primary; the tertiary into the secondary, etc. Thus, the iodomethylate of dimethyl aniline,  $\text{C}_6\text{H}_5.\text{N}(\text{CH}_3)_3\text{I}$ , at  $220\text{--}230^\circ \text{C}$ ., gives the hydriodide of dimethyl toluidine:



and the latter, heated still higher, gives hydriodide of methylxylidine,



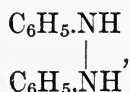
and at  $335^\circ \text{C}$ . there is formed the hydriodide of trimethyl-amido-benzene:



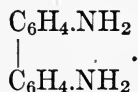
This isomerization may be explained by a dissociation of the ammonium derivative and the action of  $\text{RI}$  on the compound. The  $\text{R}$  group takes the ortho or para position with reference to the nitrogen, but never the meta.

Pyridine compounds behave in the same manner when heated:  $C_5H_5N.C_2H_5I$ , heated to  $320^\circ C.$  for some hours, is converted into the hydriodide of ethylpyridine,  $C_5H_4(C_2H_5)N.HI$ . This method is applied to the preparation of the homologues of pyridine.

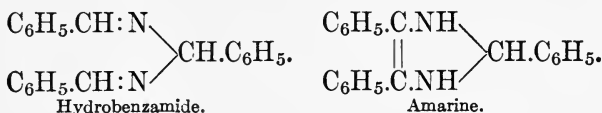
Isomerization affords a method for the synthesis of the diamine derivatives, starting from the hydrazo compounds.<sup>1</sup> Thus, hydrazobenzene,



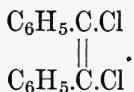
under the influence of acids, gives benzidine:



In the same manner, hydramines, heated to  $130^\circ C.$ , or by boiling with potash, are converted into a stable nucleus:



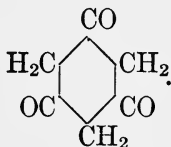
An interesting fact is the reciprocal transformation by heat of the two isomers of dichlortolane, using  $63^\circ$  and  $143^\circ C.$ :



<sup>1</sup> By the action of energetic reducing agents on azo bodies, which give hydrazo-compounds, the latter isomerizing as above.

This isomerization, along with others (fumaric and maleic acids, etc.), can only be explained by considering the spatial relations of the atoms in the molecule, and by admitting, with Wislicenus, that one of the isomers is plano-symmetrical and the other axio-symmetrical.<sup>1</sup> In these cases, as with dichlortolane, where two different bodies are represented by the same formula, the isomerization is called tautomerism. When one and the same body is decomposed differently under the influence of different chemical agents, a single formula does not suffice to explain its reactions; two formulas are required, giving a different distribution of the atoms in their spatial relations in the molecule. Thus, aceto-acetic ester,  $C_3H.CO.CH_2.CO.OR$ , under certain conditions behaves like a compound having the formula,  $CH_3.C(OH):CH.CO.OR$ .

Phloroglucol (trioxy-benzene 1:2:4) sometimes behaves as a triketone:



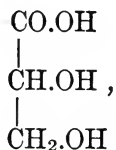
Optically inactive substances (but containing an asymmetric carbon atom) can be converted into different isomers by different decompositions. The simple crystallization of the salts is sometimes sufficient, as in the case of tartaric, malic, phenylglycollic acids, etc. In the same manner, artificial  $\alpha$ -propylpyridine (the salt) gives an isomer which rotates the plane of polarized light to the right.

This double nature appears to disappear when one or several isomers are mixed together, when the different rotatory powers mutually annul one another.

The splitting-up of a substance into two isomeric bodies may sometimes take place through the agency of a micro-organism which will destroy one of the isomers. Thus, with amyl

<sup>1</sup> See *Bull. Soc. Chim.*, vol. 49, p. 457.

alcohol,  $\text{CH}(\text{CH}_3)(\text{C}_3\text{H}_7)\text{OH}$ , there is formed, by the aid of ferments, a lævo-gyrate alcohol. Glyceric acid,



behaves in the same manner. With conicine, there cannot be obtained by this method the optically active isomers, on account of its destructive action on inferior organisms.





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